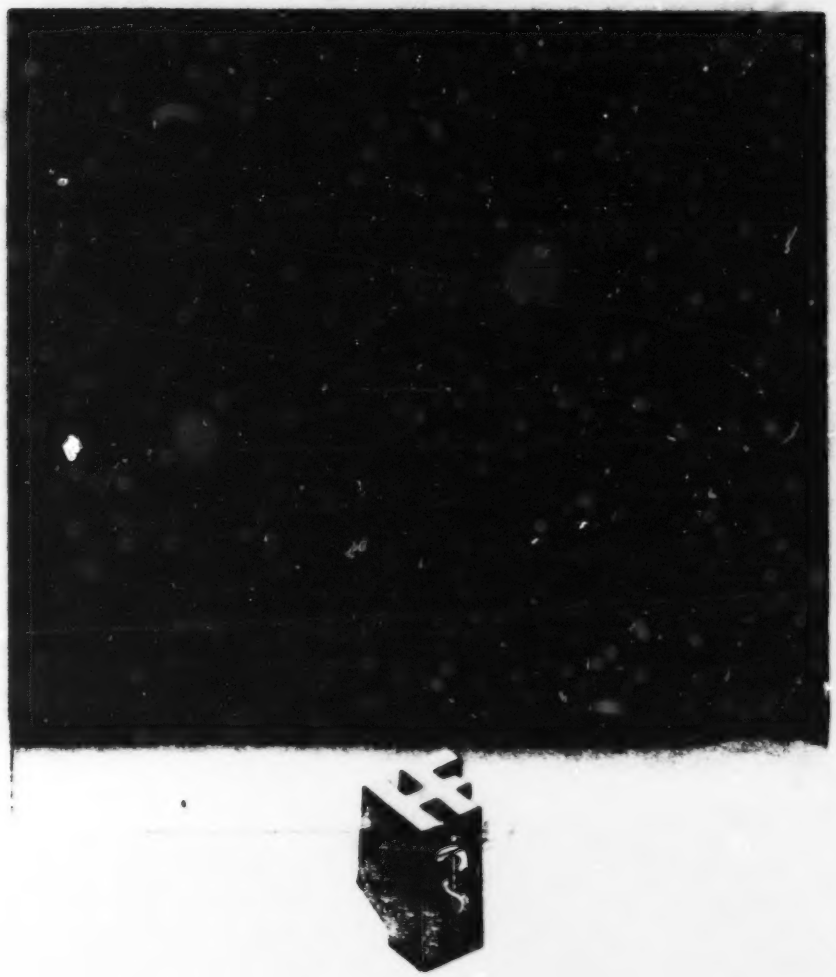
ALBERTA HERITAGE FOUNDATION FOR MEDICAL RESEARCH



THE THIRD ANNUAL REPORT
THE TRIENNIAL REPORT 1980-1983

The Foundation's Story: A Brain Industry

President's Perspective

The Researchers – Life in the Lab

18-5034

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AN OVERVIEW

In November 1979 an Act of Legislature created the Alberta Heritage Foundation for Medical Research to establish and support a balanced, long-term program of medical research based in Alberta. Foundation activities are directed toward the discovery of new knowledge and the application of that new knowledge to improve health care of Albertans and all people.

To build a balanced program, the Foundation supports basic and clinical scientists, both well-established people and young people beginning new research careers. Investigators explore a broad spectrum of disciplines such as: biochemistry, microbiology, pediatrics, immunology, neurology, dentistry, pharmacology and many others.

The Foundation is supported by a $300 million endowment fund which generates interest revenue for operating expenses. The Foundation stands at arm's length from the government under the management of a group of distinguished Trustees.

The long-term nature of medical research is recognized in the fact that a detailed report of activities is required triennially. This is the first Triennial Report and also the third Annual Report submitted to the Legislature. Every six years the Foundation's work will be reviewed by an International Board of Review.

AWARDS AND GRANTS

The main activity of the Foundation is an awards and grants program designed to establish a critical mass of career scientists in Alberta. The program includes:

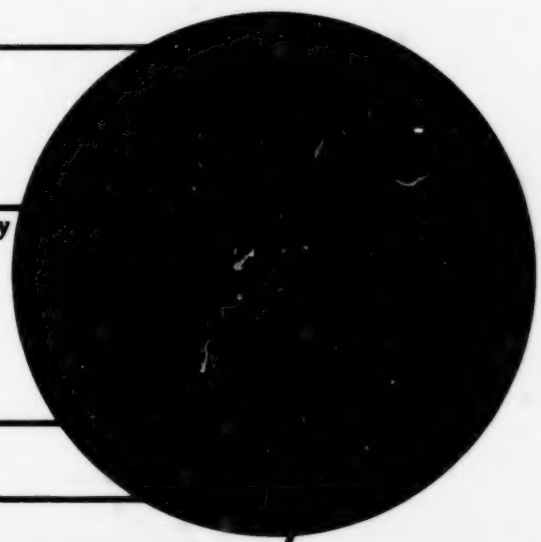
- Heritage Medical Scientist and Scholarship Awards
- Studentships (full-time, part-time, and summer)
- Fellowships
- Establishment Grants for New Investigators
- Grants for Major Equipment
- Grants for Equipment Maintenance
- Research Professors-in-Residence
- Visiting Scientists to Alberta
- Visiting Scientists from Alberta
- Visiting Lecturers
- Visiting Professors
- Travel Grants
- Grants for Conference Support

Much of the Foundation's work is carried out on the advice of a Scientific Advisory Council with 13 members who represent the national and international medical scientific communities. The international nature of the Council ensures quality peer review according to the highest standards and facilitates ongoing communication with researchers throughout the world.

The Council and its committees review and advise the Foundation on applications for loans, grants, research projects and professorships.

AHFMR Expenditures 1980-83

Total $42.8 Million



Major programs directly funding research
$24.5 M

Other programs supporting research community
7.2 M

Major equipment grants
7.9 M

Administration
2.0 M

Scientific policy and evaluation
1.2 M

To The Members of the Legislative Assembly of Alberta

I am pleased to submit the Third Annual Report, which is also the First Triennial Report, of the Alberta Heritage Foundation for Medical Research. It contains a summary of Foundation activities for the first three years of operation. We have chosen an informal magazine style for the main body of the report to enable us to communicate better to Albertans the exciting work they are supporting through the Foundation.

The Legislature established the Foundation to promote medical research and encourage excellence in the field. Looking back over the three years, the Trustees believe significant progress has been made toward that goal. This report provides substantial evidence that our mandate is being fulfilled.

I am grateful, too, for the many scientists in the medical research community who advise the Foundation and serve on its review panels, for the trustees who provide counsel, and for our President, Dr. McLeod. His expertise, enthusiasm and understanding of people and medical research gives the Foundation the outstanding leadership such a new venture requires.

I speak for all Trustees when I say it has been a rewarding experience to undertake our appointments on behalf of the people of Alberta. It's exciting to witness the enthusiasm of the medical scientific community and to receive its positive comments and helpful advice.

On behalf of the Trustees,

Eric A. Geddes

Eric A. Geddes
Chairman

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Dr. Aser Rothstein, Professor of Medical Biophysics, Director of Medical Research Institute, The Hospital for Sick Children, Toronto, Ontario

Dr. David L. Sackett, Professor, Department of Clinical Epidemiology and Biostatistics and Medicine, McMaster University, Hamilton, Ontario

Dr. Rene Simard, Scientific Director, Institut du Cancer de Montreal, Centre Hospitalier Notre-dame, Montreal, Quebec

Dr. Warren L. Veale, Professor and Head, Department of Medical Physiology, Faculty of Medicine, The University of Calgary, Calgary, Alberta

A BOLD MOVE

Creating the Alberta Heritage Foundation for Medical Research was a bold move. The goal was extraordinarily ambitious – to make Alberta a world centre of medical research. At the time, 1979, medical research in the province was underdeveloped with little activity and only a scattering of scientists producing work of international calibre.

The decision to establish the Foundation was not a conventional investment. It was an investment in knowledge and brainpower. Alberta would keep her best scientific minds at home and attract more of the world's finest. They would generate new knowledge to be translated into better health care for Albertans and ultimately people everywhere.

It's happening. Three years later, through careful planning and unprecedented levels of funding, Alberta is on the way to becoming a world centre of medical research.

The establishment of the Foundation in 1979 was the result of several years of discussion and planning on the part of Alberta's medical schools and the Government of the Province of Alberta. The medical schools had long advocated strengthening medical research in Alberta to improve medical education and practice. The Government recognized the increased frailty of medical research funding and the limited existing resources of Alberta. The concept of the Foundation emerged when the Government launched an extensive investigation of research funding institutions throughout the world. Dr. John E. Bradley headed this investigation and later became the Foundation's first Executive Director.

International, Canadian and local scientists all emphasized the same critical points in their advice to the Government. Scientists needed long-term funding and the freedom to conduct creative and innovative projects. If Alberta wanted to establish a solid, yet exciting research community it needed to do two things: attract a cadre of esteemed scientists who would spark one another as a "critical mass" was formed, and create more opportunities for young people to enter medical research careers and receive high-quality training.

A GROWING SCIENTIFIC COMMUNITY

The Foundation has been meeting these two objectives. Some of the best people have been recruited for Alberta's new "brain industry". In three years, over 49 scholars have come to Alberta, or chosen to remain here, because of the availability of five-year renewable awards and ample start-up funds for technical staff, state-of-the-art equipment and laboratory space. Once the medical scientist has proven his or her potential in a rigorous peer review and evaluation system, the Foundation has said, "You are well-trained and have the potential for important productivity. You have the freedom to explore your chosen hypothesis within the community of other researchers."

No magic number or point in time will define a critical mass of investigators, but substantial progress has been made. Alberta is attracting new interest on the part of others from Canada and elsewhere.

A variety of programs support young researchers in training: 961 were funded as of March 1983. Awards range from Summer Studentships to Establishment Grants for newly graduated investigators. High school students are introduced to medical research through a program supporting Alberta's Regional School Science Fairs. The Foundation sponsors awards of excellence and the award-winning students visit laboratories of Heritage-supported scientists.

AN INTERNATIONAL NETWORK

Other programs enhance the research climate in a variety of ways. Visiting Scientist Awards bring lecturers and professors from all over the world to The Universities of Alberta and Calgary. These researchers give first-hand accounts of research progress, directions and new technology. Similar grants fund travel by Alberta investigators so they can present their findings to the international scientific community, gain experience in other laboratories and attract interest in Alberta's research thrusts. Foundation support of national and international scientific conferences also fosters communication among scientists and highlights Alberta's role.

An extensive Equipment Program has modernized Alberta's medical research laboratories and provided existing and new scientists with critical technical support. During the first three years, the Foundation has evaluated 290 applications requesting funds for major medical scientific equipment. Of these, 198 applications were approved and close to $8 million granted.

In establishing programs, awarding grants, reviewing progress and creating operational policies, the Foundation has sought the advice and criticism of the medical scientific community. The Foundation is grateful for this valuable assistance which is so essential to the quality of all programs.

Given the initial bold move and the time required to build an organization, what has the Foundation funded? The projects cover a mind-boggling vari-

ety of clinical and basic research with studies in: genetics, respiratory and gastrointestinal systems, pharmacokinetics, oncology, endocrinology, nutrition, immunology, the biomechanics of exercise and biomaterials in dentistry. Several areas of impressive strength have emerged and are attracting other new scientists: cell regulation, the neurosciences, cardiovascular medicine, infectious diseases, microbiology and genetics. Projects like the virology studies are exciting because they may lead to the prevention of disease.

FOUNDATION A CATALYST

During the first three years of careful planning – and some eager scientists would say the Foundation has been frustratingly slow – several potential problems have been worked out. In the beginning some speculated Alberta researchers would be disadvantaged in national and international competitions. But Foundation funding has complemented, not competed with the work of other agencies. The presence of the Foundation has enhanced medical research in Alberta and attracted more outside money, not less.

There were other concerns about how the universities would respond to Foundation opportunities. However, a partnership has been satisfactorily worked out, evidenced by the number of scholars put into place. These scholars have added strength to instructional staff. All programs have been implemented cooperatively, and the Foundation has provided funds for renovated space.

Clearly, the medical schools have acquired increased status in the research community. According to the Association of Canadian Medical Colleges' rating (status is based on research dollars) The University of Alberta moved from eleventh position in 1978 to fifth in 1982. The University of Calgary moved from fifteenth position in 1978 to ninth in 1982.

This realignment of Alberta medical schools in research budgeting reflects the increased funds provided by both the Foundation and the National research granting agencies. From 1980 to 1983, research funding at The University of Alberta increased by 47% (from $29.95 to $43.93 million). Funding by the Medical Research Council of Canada increased by 20% and by the Natural Sciences and Engineering Research Council of Canada by 33%. Over the same period, research funding at The University of Calgary increased by some 90% ($14.04 to $26.55 million) and from the Medical Research Council of Canada by 57% and the Natural Sciences and Engineering Research Council of Canada by 55%. With an annual budget of $25-$30 million, the Foundation is now a major sponsor of medical research at The Universities of Alberta and Calgary.

NEW DIRECTIONS

Now that the inevitable growing pains of the first three years are over, Foundation activity is accelerating. The future will see even more scientists put into place, an estimated 40 more by 1985. New activity will focus on two new directions.

There is a shortage of space for laboratories at the universities. While there is limited space for individual scientists, there is almost no vacant space for major new groups similar to the NMR and cell regulation groups already established. Therefore, the Foundation is considering allocating substantial amounts of unexpended endowment interest for the construction of new facilities.

Secondly, Alberta, like other medical research centres in North America, has a serious shortage of well-trained clinical scientists who directly study patients and patient problems. The Foundation is designing new programs to provide incentives and learning opportunities for young clinicians. If clinicians are given attractive research arrangements and competitive research skills, they will be able to investigate the effects of old and new drugs and the usefulness of other new treatments. This program will further the Foundation's objective to achieve a balanced program of medical research.

The dream of Alberta as a world centre of medical research is being realized. The numbers of scholars in place – Albertans previously working in the province, returned expatriates and new recruits from all over the world – are one proof of progress. Significant numbers of young people entering and continuing in research careers are further evidence. Less concrete, but equally revealing is the response of people within the scientific community. Scientists here and abroad say over and over, "Alberta is now a very exciting place to be."

THE PRESIDENT'S PERSPECTIVE

An interview with Dr. Lionel McLeod

How do you feel about the Foundation's accomplishments in its first three years?

The Foundation has accomplished a great deal given its starting point – the fact that it required organization, that it needed to establish its granting programs yet it has supported an impressive number of new medical scientists in Alberta.

Considerable progress has been made in the area of recruitment of new scientists to Alberta but the area needing much more development is clinical research.

Why has Alberta been so successful in recruiting researchers?

Largely because the Foundation provides a unique funding opportunity for new scientists, an opportunity not matched anywhere else at this time. Very few new medical research positions are accompanied by start-up funds that provide a full range of equipment and laboratory facilities for students and fellows. These are some of the factors that result in a unique opportunity in Alberta. The enthusiasm of the established medical research community is also a very important factor.

"Supported by the Scientific Advisory Council, the Foundation has decided to fund the best research ideas and the best people irrespective of the discipline."

How do you decide who to fund? How can you be sure your awards truly represent quality and future potential?

The Foundation employs techniques developed in North America and elsewhere over the last 20-25 years. Multidisciplinary groups of researchers screen applications and experts within the specific field of the research application also provide evaluations. By combining these two and minimizing bureaucratic evaluation, we believe we achieve the best assurance of quality. Let me use an example – suppose we receive an application from a scientist in microbiology, perhaps one concerned for the incidence of certain childhood infections. The application will contain a certain amount of structured information. It will be forwarded to experts in that particular area of research wherever they may be found in the world. The expert or external referee is asked to provide an evaluation of the skill of the applicant and appraise the potential significance of the new information; for instance, whether the project is repetitive, innovative and on a frontier of research. The reports of the external referees – and there may be three or four of them – are then presented to a panel of researchers from a range of disciplines who provide a final assessment on the worthiness of the project, the applicant and the probability of beneficial impact on Alberta's research development. Should these two levels of evaluation mesh, then a recommendation to fund the applicant goes forward to the Trustees of the Foundation.

Do you feel the Foundation is under any sort of pressure, either from the public or government, to fund certain areas of research? For example, in the United States cancer research has been a very popular thrust.

That is a good question because it is perfectly reasonable for the public, either individually or in groups, to call upon granting agencies to solve specific problems. Unfortunately, a great deal of money can be spent pursuing problems where the basic information, the background understanding, is insufficient to allow significant research progress. Money can also be misspent attacking questions without an innovative approach. Supported by the Scientific Advisory Council, the Foundation has decided to fund the best research ideas and the best people irrespective of the discipline. If you examine major research breakthroughs of the past, you will find they often arose in unrelated areas when scientists were working at a distance from the actual disease problem. It seems most useful to fund well-trained, very bright people who come up with new and creative ideas.

Does the Foundation compete with other funding agencies like the Medical Research Council of Canada or the Canadian Heart Association?

Only in a very limited and quite acceptable way. Those agencies concentrate primarily on so-called operating grants. An operating grant provides funding for technicians, chemicals, materials and supplies and so forth. In Alberta, the Foundation has concentrated on providing student and staff research positions and people in these positions require operating funds from other agencies. This way we create pressures upon those other agencies in a complementary way. The Foundation is collaborating with these various agencies to enhance Alberta's contribution to medical research. The increasing quality and scope of research here has attracted more outside funds, not less.

How serious is the weakness in clinical research in Alberta? What is the Foundation doing to redress the imbalance between clinical and basic research?

Two questions. The first deals with our current state of affairs. Alberta has always had competent clinical researchers but in insufficient numbers to allow the kind of progress characteristic of better developed centres.

The Foundation's newly designed program will increase the training and recruitment of new clinical researchers to create a critical mass in Alberta. The quality and scope of clinical research is a concern across the whole of North America. Fewer young people are prepared to take the extensive

time required to become both a clinician and a researcher. Our programs offer medical school graduates improved financial support which hopefully will encourage them to enter research careers. This should allow us to improve the balance of medical research in Alberta. Scientists will be able to address problems at the cell and sub-cellular level, and simultaneously ensure the communication of new information to the clinical researcher working on actual patient problems. That transfer should increase the chances of bringing about direct benefits to patients.

Is the Foundation accountable to the public?

The Foundation certainly is accountable to the public as it spends monies gained from the interest produced by its endowment within Alberta's Heritage Trust Fund. The Foundation is also accountable to the public through our universities by the fact that the funded scientists are members of the university community in the main. The Foundation's activities may be examined in annual reports which are provided to members of Alberta's Legislative Assembly. Finally, and importantly, our Trustees are representatives of the community at large.

All of the scholars are monitored for the quality of their productivity through annual observation of their activities, especially as those activities are reviewed by the medical scientific community. A formal review with detailed reporting occurs every five years.

Has the Foundation managed to avoid being bogged down by bureaucracy and administrative expenses?

I believe so though not all would concur with my view on the issue of bureaucracy. We have done very well, according to reports I have received, though the multidisciplinary and external peer reviews take time. Our administrative costs have been well-contained, perhaps to a level that produces some delays in evaluations and in analyses of our activities. With limited staff, the Scientific and Financial sections work hard and well and have accepted their responsibilities in exemplary fashion.

We depend heavily on assistance from large numbers of medical scientists both from within and without Alberta. This assistance is provided with nominal honoraria. In this way, applications for Grants and Awards receive careful scrutiny and appraisal for merit and the value of the investment made by the Foundation.

Another advantage is that our main objective deals with the recruitment and establishment of new scientists. The Foundation does not face the difficult problems of evaluating operating grants required for the ongoing performance of research. Those funds are sought by our scientists from other agencies. This is a direct result of the Foundation's objective to considerably enhance the medical scientific community of the Province of Alberta.

When will Albertans see the impact of the Foundation?

There are probably two ways to answer that question. Firstly, I think Albertans should be aware that there is now an important impact in that the total amount of new information in medical sciences being produced in Alberta and transmitted to the rest of the world has increased significantly. This results directly from the productivity of some 49 or more scientists who have been recruited and established in Alberta. Secondly, many of these new medical scientists have contributed clearly and directly to the quality and diversity of Alberta's specialty patient care programs found within those clinical care areas. One could cite developments in infectious disease, problems of the lungs and heart, genetics, the neurosciences, gastrointestinal disorders and others.

What do you expect in the next five years?

Firstly, and naturally, we will pursue with vigor the attraction of able new medical scientists to Alberta. From this continued recruitment I anticipate the emergence of significant major groupings of medical scientists along with accelerated growth of research activity. As the result of new programs, I am hopeful that clinical, patient-oriented research will flourish as young people are drawn into sound programs of training and the clear opportunities offered by the Foundation's new programs. Clearly, we all hope the outcome will be a broadly-based, first-class centre of medical research in Edmonton and Calgary.

As first President of the Foundation, what do you find most satisfactory?

Seeing the new opportunities for young Albertans to test themselves against the rigorous requirements of medical research; and experiencing the enthusiasm and quality of new scientists establishing themselves in Alberta. All this after the arduous and slow, though successful, development of the past 15 years.

Finally, the spin-off! The rejuvenated spirit and enthusiasm of people who have worked in Alberta over the years, enthusiasm generated by contact with students, fellows and new colleagues.

Dr. Lionel McLeod, President

"On a per capita basis nothing like this has happened in the history of science before anywhere – not only in Canada or North America but anywhere. No population of scientists has ever been given the kind of opportunity that we have in Alberta. With that opportunity comes an incredible responsibility."

Dr. George Drummond
Member, Scientific Advisory Council

SCIENTIFIC ADVISORY COUNCIL PLAYS KEY ROLE

These comments convey the sense of excitement and responsibility felt by members of the Scientific Advisory Council, a key part of the Alberta Heritage Foundation for Medical Research.

The Council, made up of 13 internationally respected scientists from Canada, the United States and Britain, advises the Foundation on policy and programs. Members have extensive experience with funding agencies and with development of special areas of medical research. They also have an awareness of which research areas will be most fruitful or relevant in the future.

In addition to its advisory role, the Council is active in developing new programs – for example, the Heritage Medical Scientist Program. The program is designed to recruit well-established, internationally recognized investigators to Alberta who will contribute to both the quality and productivity of Alberta medical research and to the education of future medical scientists. The Council has also been active in exploring ways to stimulate research in clinical areas:

In speaking with Council members, it becomes clear that they welcomed the chance to be involved with the Foundation. "I accepted a position on the SAC because the Foundation is one of the most exciting and promising adventures I have seen in academic medicine in North America," says Dr. James Maloney, Professor of Surgery at The University of California Medical School in Los Angeles.

Dr. Ernest McCoy, Professor and Chairman in the Department of Pediatrics at The University of Alberta, feels the non-Albertans on the Council make an important contribution. "They bring in ideas from other places," he notes. "For example, they have offered valuable ideas for stimulating clinical research."

To ensure that the Foundation makes the most beneficial contribution possible to medical research, the Council relies on the cooperation of other granting agencies, institutions and individuals from around the world. The co-operation is definitely there, says Council member Dr. Warren Veale, Chairman of the Department of Medical Physiology at The University of Calgary. "We have the support of other agencies, including the MRC (Medical Research Council) and our international contacts are good."

While the 13 individuals on the Council have differences of opinion, Dr. George Drummond, Professor of Biochemistry at The University of Calgary, sees this as inevitable – and not a barrier to progress. "There's an enormous amount of goodwill on the Council. We're all trying to do the best job we can."

WORLD'S FINEST ATTRACTED TO ALBERTA

When Dr. Joe Davison came to The University of Calgary in 1981 as a Heritage Visiting Scientist, he had no plans for staying on past his sabbatical year. However, so impressed was Davison by the environment in Calgary that he decided to leave his position at The University of Dundee in Scotland for one in Alberta.

For Dr. Wai Choi Leung, moving to The University of Alberta meant that he could establish, in a very short time, a laboratory that was double the size of his laboratory at McMaster University in Hamilton.

Davison, a physiologist, and Leung, a virologist, are both world-class researchers who are here because of the Alberta Heritage Foundation for Medical Research. To investigators like Davison and Leung, the Foundation offers two vital benefits: stable, long-term funding and a highly active and progressive research community.

In the case of Davison, who was adequately funded at The University of Dundee, the primary attraction was the environment at The University of Calgary.

"I found, after even just a few weeks of working here, that the general approach, the attitude and the enthusiasm for what was happening became quite contagious."

A basic scientist, Davison also appreciated the opportunity for collaborative work with colleagues in the gastro-intestinal research group. "I have several projects under way with clinical colleagues and they're proving productive too."

Because of Foundation support, Leung points out, Alberta is the only place in North America where an investigator can become productive in a very short period of time. "Through the studentship, fellowship, major equipment and establishment grant programs, the Foundation provides important support," he stresses.

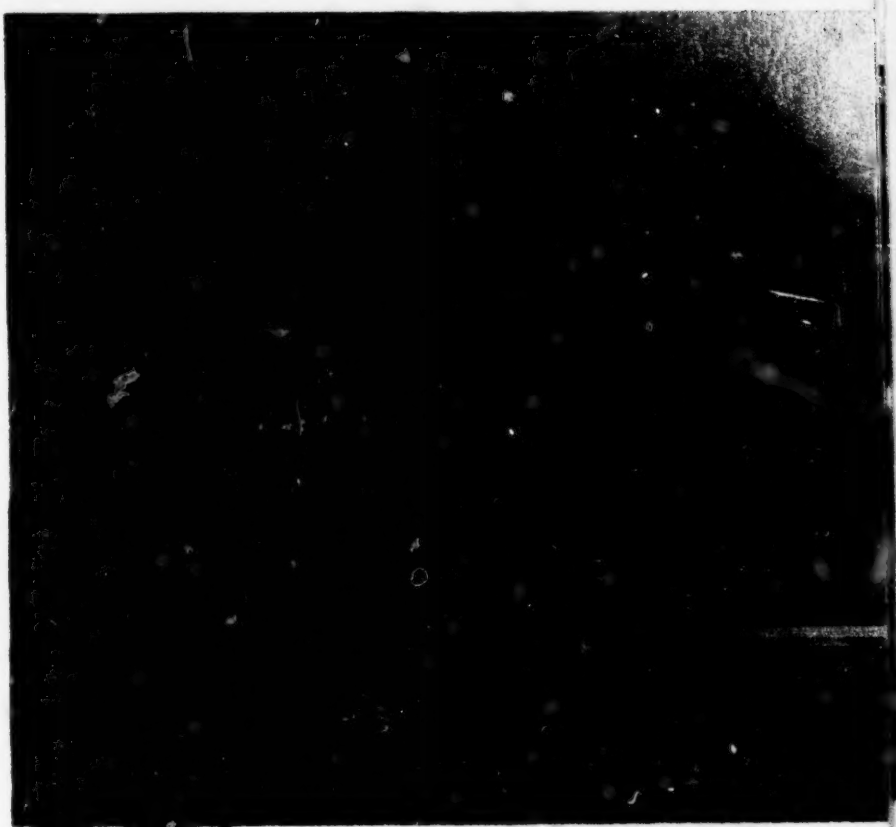
The skill of the scientists with whom he could collaborate – particularly those in the protein chemistry group in the Department of Biochemistry – was also crucial in attracting Leung to Alberta.

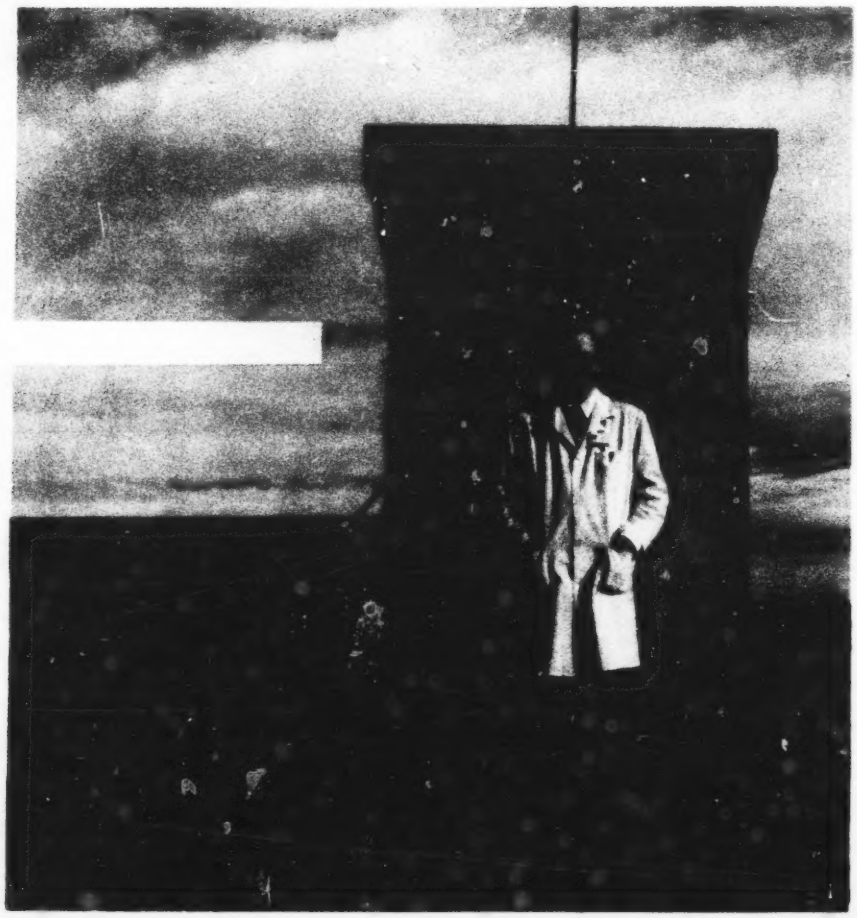
"I detected a real opportunity here," says Dr. John Tyberg, who left the United States to join the Cardiovascular Respiratory Research Group at The University of Calgary. "The Cardiology Division was small, but there was good leadership and the commitment to grow."

Since Tyberg's arrival in Calgary in July of 1981, growth in the Cardiology group has indeed occurred (see story on page 22), and Tyberg attributes this growth largely to the Foundation's support.

For the investigator who wants to make research a lifelong career he notes that the Foundation offers the possibility of protracted funding.

Dr. Joe Davison, a physiologist at The University of Calgary, heads a laboratory team that is studying nervous control of gastro-intestinal functions. More specifically, Davison and his colleagues are looking at the control of secretion in the gastro-intestinal tract by certain nerves. They are also studying electrical changes occurring in cells during the secretion process. Davison's research is relevant to the treatment of many gastro-intestinal defects, such as peptic ulcers, inflammatory bowel diseases and cystic fibrosis.

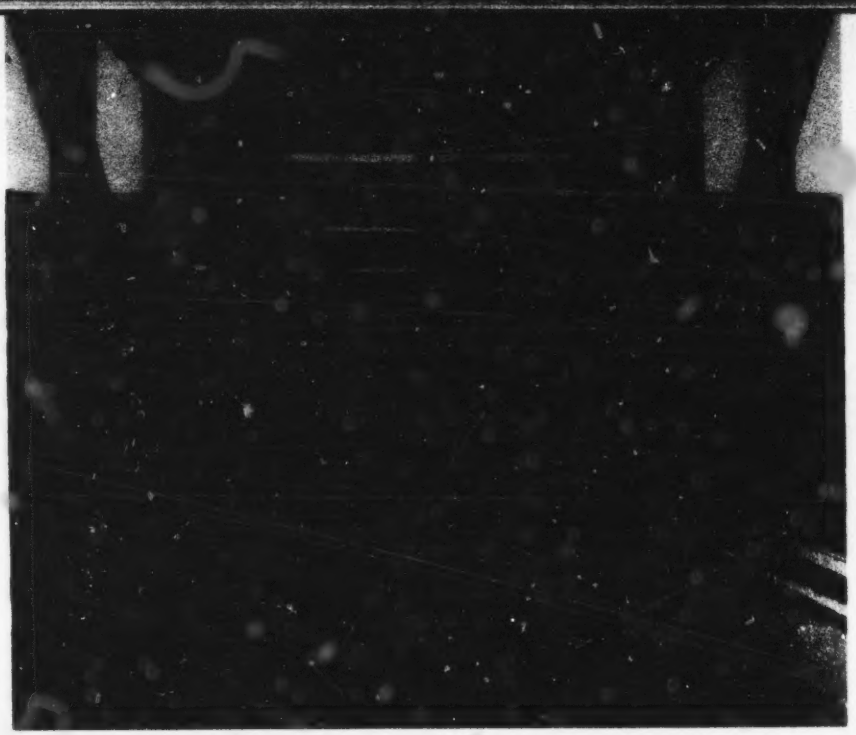




Dr. Wai Choi Leung, a virologist at The University of Alberta, is working to make new vaccines available for virus-induced diseases, particularly the herpes simplex virus. In addition to standard recombinant DNA technology, Leung uses a new technique for chemical DNA synthesis, an important step towards developing viral vaccines as well as producing other useful pharmaceuticals through bacteria or yeast. Leung describes his highly competitive research area as a "hot topic" all over the world. "We have to work fast," he says. "There is an urgent need for an effective herpes simplex virus vaccine."

For a long time doctors have used the level of pressure in the left ventricle during the resting phase as a basis from which to assess the heart's performance. Conventionally, if this pressure was abnormally high as it is in heart failure, doctors assumed that the left ventricle was stretched and probably working at its optimal size. Naturally they feared that when this pressure declined significantly, as it does when heart failure is treated successfully, the heart also became much smaller and thus less effective. **Dr. John Tyberg** and his colleagues at The University of Calgary have discovered that during heart failure the left ventricle becomes compressed by structures around it; this external pressure can be caused by the pericardium, the sac around the heart. When therapy for heart failure reduces the resting pressure in the left ventricle, most of the reduction is in this external pressure and therefore does not indicate a reduction in size and effectiveness. With this understanding based on Tyberg's work, cardiologists will be better able to optimize the performance of the diseased left ventricle.

Alberta is becoming a world leader in Nuclear Magnetic Resonance (NMR) – an exciting new way of imaging the body and studying bodily processes. **Dr. Peter Allen**, an NMR physicist from The University of Nottingham in England, is a member of The University of Alberta's NMR team. "The support of the Foundation – which is so much better than the level of funding in the United Kingdom – allows me to explore problems I'm interested in solving. In addition to straightforward imaging, I look forward to studying the use of NMR to investigate body chemistry because I think it will prove to be more fruitful."



1 Dr. John Tyberg
2 Dr. Wai Choi Leung
3 Dr. Peter Allen
4 Dr. Jerry Wang

Dr. Jerry Wang came from The University of Manitoba to join The University of Calgary's dynamic Cell Regulation Unit. As its name indicates, the group is interested in the process by which living cells regulate what they do, both in metabolic and physiological functions. Wang, who is primarily known for his groundbreaking work on calmodulin (a calcium-binding protein) was attracted to Alberta because of the people and the energizing atmosphere. "I was looking for new stimulation and there is probably no better place than Alberta because of the high level of activity with the Foundation. The general spirit is so much higher here than anywhere else in the nation."

JOINING THE REVOLU

Researchers in molecular biology know they are in a revolution. It's a revolution that goes right to the very source of life – the cell – and one that charges investigators with energy and a high level of dedication.

"We're in the midst of constantly questioning how we think about cells, biology and all living things," says Dr. Grant McFadden, one of the Foundation's Heritage Scholars working in The University of Alberta's Department of Biochemistry.

If the human body is going to malfunction in some way, it's going to start happening in a cell – and researchers like McFadden are determined to achieve a greater understanding of that complex, microscopic environment.

AN EXPLOSION IN KNOWLEDGE

Undoubtedly the most important factor in precipitating this revolution in biology was the explosion in knowledge about DNA that began in the 1950's. Greater knowledge of DNA, the molecule that carries the genetic code from one generation to the next, has led to the DNA cloning and recombinant DNA technology that are central to the revolution.

DNA cloning means that researchers can take the DNA of advanced organisms and grow specific pieces (individual genes) in large bacterial cultures that have many life cycles – thus making experiments possible that were impractical before the advent of cloning technology.

Recombinant DNA technology allows researchers to artificially manipulate the structure of these pieces of DNA to understand their function. With this technology, researchers are gaining a greater understanding of biological processes, as well as what makes congenital diseases or cancer possible.

THE "BLACK BOX"

It's searching for solutions to problems that keeps McFadden an openly enthusiastic molecular biologist.

"I'm a problem-oriented person. I like black boxes," he tells you in a small office of his laboratory.

McFadden's "black box" is the genetic structure of a particular tumor-causing virus that occurs naturally in some animal species. Ultimately, his laboratory team hopes to provide a model for understanding tumor formation in humans. By studying normal and viral-infected cells in tissue culture, McFadden and his colleagues are trying to find what the virus does to trigger the cellular switch that causes tumors.

"Viruses, chemicals and ionizing radiation are all environmental agents that have targets in cells that can be switched on to cause cancer," he explains. "We're looking for the cellular switch of our virus."

With hundreds of thousands of genes in cells, the virus serves as a "handle" to pull genes out of cells for study. When a gene is pulled out, McFadden and his colleagues conduct their studies using recombinant DNA technology.

THE MYSTERY OF REPLICATION

Dr. Linda Reha-Krantz, a Heritage Scholar in the university's Department of Genetics, is also making regular use of recombinant DNA technology.

Reha-Krantz is searching for the answer to one of science's most persistent mysteries – how a living organism, be it a virus or human being, a skin cell or heart cell, duplicates itself accurately. The secret to the mystery lies somewhere in the complex biochemical process by which DNA replicates itself.

"If we can understand how DNA is replicated and repaired in more detail, this can give a basis for understanding a range of diseases," says Reha-Krantz.

TION

The key to the replication process is the DNA polymerase, one of 10 to 15 proteins required for DNA replication. Reha-Krantz has devised a method of isolating mutant DNA polymerases of bacteriophage T4 (a virus which infects bacteria). These mutants are defective and make many mistakes in the replication process.

By studying these mutants, Reha-Krantz hopes to use them as a jumping off point for eventual experiments with more advanced organisms. However, she cautions that "the replication process is very complex in T4 and it's a safe bet that it won't be any simpler in humans".

In addition to the study of DNA replication itself, Reha-Krantz is also keenly interested in advancing the biotechnological methods in her field – that is, the methods of making mutations in DNA. This important by-product of her research, she stresses, could produce advances in everything from agriculture to medicine.

LITTLE EUREKAS

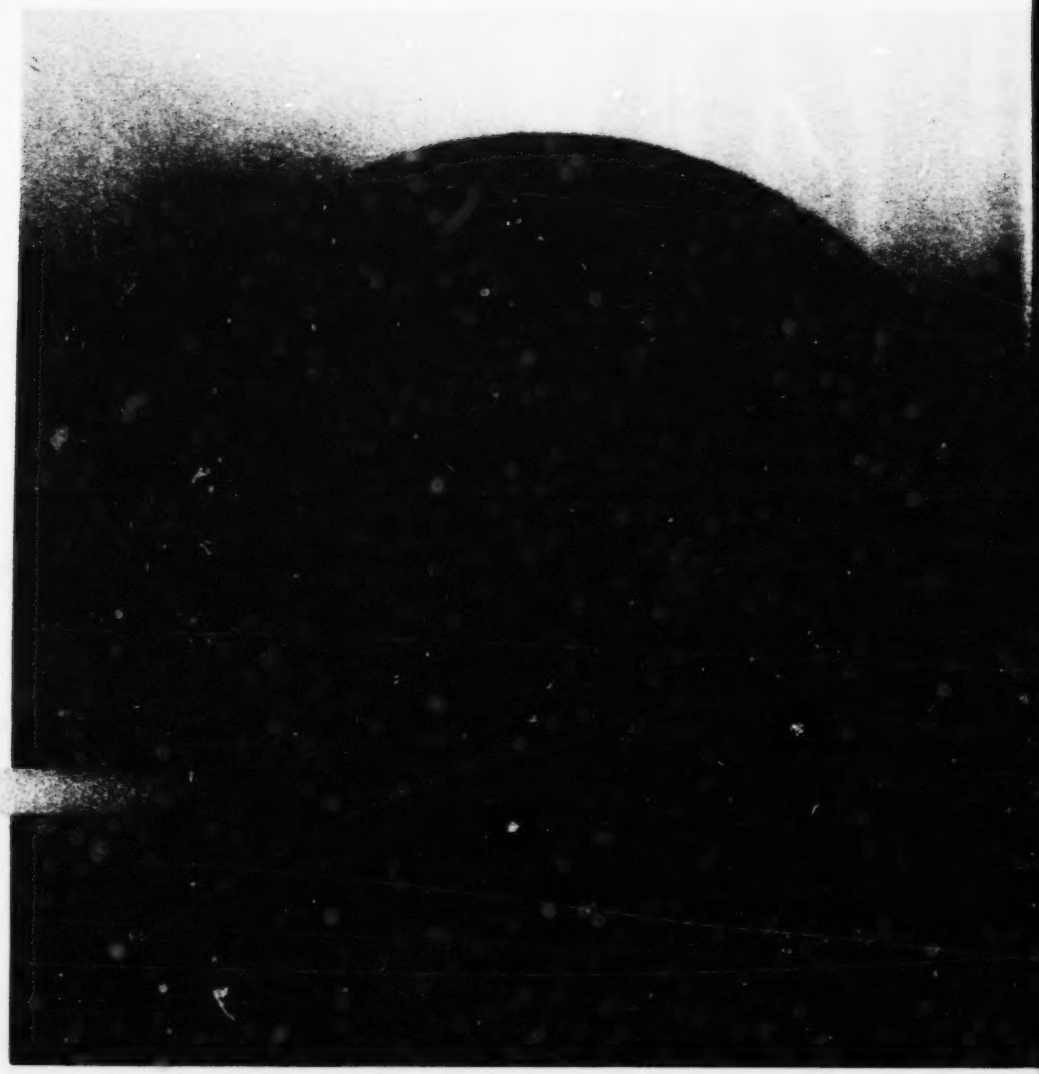
The type of basic research that scholars like McFadden and Reha-Krantz are undertaking is absolutely crucial, says Dr. John Colter, Chairman of the university's Department of Biochemistry and a member of the Foundation's Scientific Advisory Council. A researcher himself, Colter notes: "In the final analysis, a real understanding of the underlying mechanisms of disease will only come from basic research."

It is basic research, he adds, that can provide the knowledge for practical development. For example, studies in basic physics led to the development of x-rays. But it will take a combination of many individual efforts to achieve the advances for which so many are so anxious.

"Real advances don't happen with big eurekas. There are a lot of little eurekas," says Colter.

At The University of Alberta, Dr. Grant McFadden and his laboratory team are looking for the cellular switch that "turns on" a tumor-causing virus.

ALBERTA RESEARCHERS CONFRONT THE CELL



UNIVERSITY OF CALGARY'S CELL REGULATION UNIT

PORTRAIT of a CRITICAL MASS

Scientists use a special expression when they want to convey that things are going well, that a first-rate team of researchers has come together. They speak of a "critical mass", and it means that there's enough assembled brain power to produce some highly respectable work.

One critical mass – whose establishment was made possible through Foundation support – is the Cell Regulation Unit at The University of Calgary.

The unit's formation was spearheaded by its chairman, Dr. George Drummond, who began talking to scientists who could help create a world-class group some four years ago. A crucial boost came when Dr. Jerry Wang, a scientist of world renown, left Manitoba to come to Calgary

in January of 1983, joining Drs. David Waisman, Michael Walsh and David Severson. Dr. John Northup joined the team in May of 1983.

According to Wang, the Foundation's support was vital in making the formation of the Cell Regulation Unit possible.

"I'm sure that without the Foundation this group would not have been formed," he says.

Wang particularly appreciates the interaction that is possible with a critical mass. The unit is an interdisciplinary mix that includes pharmacologists, protein chemists and physiologists.

"People in the research business never work alone," Wang notes. "They always have to interact with other people, through meetings, calls or reading about each other's work. But the best interaction is still person-to-person." The individuals in the Cell Regulation Unit complement each other, he adds, not only in techniques but in their special areas of research.

Dr. John Northup, who came from The University of Texas Health Sciences Centre at Dallas to join the unit, is equally enthused about possibilities for interaction. "We can activate things. We exchange ideas. We synergize."

With an energetic and dedicated critical mass now in place, Northup is convinced that the years ahead will be productive ones. "This group will go far," he says confidently.

The unit's basic research interest is the process by which living cells regulate what they do, both in metabolic and physiological functions; or, put another way, how cells respond to outside stimulation.

"We're particularly interested in messengers – how the cell forms and utilizes messengers to turn things on and off to adjust to new physiological situations," explains Drummond.

In his laboratory, Drummond is studying a messenger called cyclic AMP, a second messenger that takes the message from the hormone (a first messenger) to the inside of the cell and turns the cellular machinery on and off.

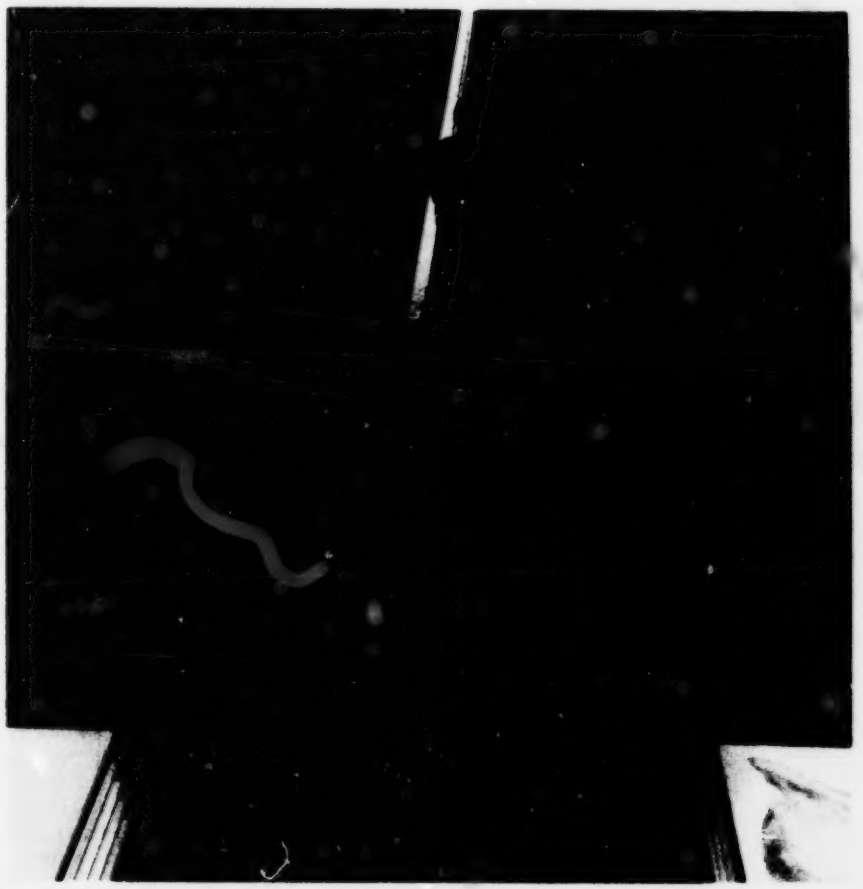
Another important second messenger is calcium, and Wang's work has been particularly important in this area. When the level of calcium in the cell increases, it bonds to a protein called calmodulin, which then becomes a strong influencing factor.

In his groundbreaking work with calmodulin, Wang purified and characterized the protein, permitting its identification with other proteins that could bind calcium and permit calcium control of physiological processes. Calmodulin plays an important role in virtually all major bodily processes, such as the cardiovascular system, the musculoskeletal system and the nervous system. Thus, Wang's research has wide applicability in understanding the healthy body and eventually diseased states.

Clearly, The University of Calgary's Cell Regulation Unit has strong potential as a research group, but breakthroughs, Drummond cautions, still require day-to-day labor.

"Science develops by gut-rending hard work at the bench," he emphasizes. "Once in a while you get a big break and the whole thing can take a giant leap forward."

Clockwise from left: Dr. George Drummond, Dr. David Waisman, Dr. Michael Walsh, Dr. David Severson, Dr. John Northup and Dr. Jerry Wang.



"Science develops by gut-rending hard work at the bench."

Looking at the inside of the human body from the outside will never be the same – and a team of University of Alberta researchers is in the forefront of that change.

It's a change that is seeing high technology backing up a world-calibre research effort. And it's a change that could revolutionize the ways of diagnosing disease.

NMR: A NEW WAY OF LOOKING

For decades, x-rays have been used to view the inside of the human body. Now, thanks to the steady advance of science and technology, researchers are working with a new, highly promising way of imaging the body called Nuclear Magnetic Resonance (NMR).

"NMR has a much wider potential application than conventional imaging techniques," says Dr. Donald Boisvert, a principal investigator on the NMR team, which was formed through Foundation support.

SAFETY AND ACCURACY

According to Boisvert and Dr. Peter Allen, the other principal investigator on the team, the non-invasive quality of NMR is one of its most important advantages.

"Conventional imaging techniques, like CAT scanning, require x-rays which penetrate the tissue and evaluate the resistance of the tissue to the rays," says Allen. "This information is then fed to a computer which translates it into an image." X-rays, he adds, aren't only potentially harmful but are limited in their application.

In contrast, NMR uses much safer radio waves in conjunction with an external magnetic field. "It's based on the principle that when certain atomic nuclei (of the body) are placed in a magnetic field, and stimulated by radio waves of a particular frequency, they will re-emit some of their absorbed energy in the form of new radio signals," explains Allen. "This phenomenon is called nuclear magnetic resonance."

The strength and the frequency of the radio signals are then fed into a computer which can translate the information into an accurate image with high contrast. NMR images of soft tissue in the body are much clearer and more accurate than x-rays or CAT scans. The NMR technique can be used for any organ of the body, generally without fear of tissue damage. (There are some exceptions, such as the complications arising from heart pacers or other metal implants.)

The non-invasive benefit of NMR isn't only limited to the absence of radiation, Boisvert points out. "NMR will permit the discontinuation of many painful diagnostic procedures. It will exclude the need for many biopsy techniques now being done, some of which are potentially dangerous."

OBSERVING BODILY PROCESSES

In addition to being less invasive than x-rays, the other major advantage of NMR is its potential for allowing researchers to study a whole range of bodily processes. This capability, distinct from NMR's imaging capability, is known as localized spectroscopy. "In spectroscopy, NMR could become a probe to identify the chemicals deep within the body, so that bodily processes can be studied in a normal state, a diseased state and under the influence of medical treatment," says Allen.

Both naturally occurring changes and changes brought about through treatments will be observable and measurable in a non-invasive way for the first time, he adds. For example, it should be possible to observe how a tumor grows, or how various drugs actually affect the function of organs. Allen stresses that localized spectroscopy is not yet "off the ground", but the University of Alberta NMR team plans to be active in its "take-off".

PHYSICAL SCIENCES TO MEDICINE

The University of Alberta team, as well as the handful of other NMR teams around the world, owe their existence to the work of pioneering scientists. NMR was first developed as an investigative technique in the physical sciences soon after the Second World War, capitalizing on the wartime advances in radar and radio engineering. Since that time, it has had many applications in physics and chemistry. Two key ingredients – a scientific foundation and a development in understanding and experimental techniques (especially in electronics and computing) – have permitted the expansion of NMR into the medical realm.

Research of this complexity requires first-rate leadership, and both of the university's principal investigators bring extensive experience to the team.

Boisvert, Associate Surgical Research Professor at The University of Alberta and Research Associate for the Cross Cancer Institute, has been involved with the NMR project since its conception. He was part of the original team of researchers from the university and the institute that formed a planning group under Dr. Brian Lentle.

Allen is an NMR physicist from The University of Nottingham in England, where he was Senior Lecturer and authority in forefront NMR research. His recruitment was a major coup for the team.

Allen's recruitment, notes Boisvert, underlines the crucial importance of basic science to much of current medical research. "We've definitely seen an increase in the complex scientific nature of the research now being undertaken, so it's not unusual to have a multidisciplinary approach."

Technologies like NMR, he adds, "are helping to transform many areas of medicine from art to science".

CANCER MAIN THRUST

Combining the strength of their interdisciplinary skills – which include physics, biochemistry, surgery, radiology and engineering – The University of Alberta team is studying NMR imaging and spectroscopy in two phases, with cancer research as the main thrust. Phase I, which began in September, will focus on developing a program of research with small animals; Phase II, running simultaneously with the first phase, will focus on clinical research with people.

Dr. Donald Boisvert (left) and Dr. Peter Allen lead The University of Alberta NMR team.

To carry out their research, the team is using state-of-the-art, medically-oriented NMR systems. The equipment, worth just over $2 million, has been custom-designed for the team's project; Allen has worked closely with the high technology manufacturers to advise them on the exact capabilities the system requires to answer research questions. The system is also being designed for maximum flexibility to incorporate future technological developments.

While the Foundation provided the funds for the equipment and some salaries, generous operating funds are being provided by the Alberta Heritage Savings Trust Fund – Applied Cancer Research. The projects are being conducted in cooperation with the Cross Cancer Institute.

Boisvert emphasizes that the team will go beyond the study of NMR imaging and cell activity (spectroscopy) – there's a keen interest in improving NMR technology itself. "Among the very few NMR research groups in the world, our interest in advancing NMR technology makes us stand out."

BRAIN POWER:

THE ATTRACTION OF A COMPLEX ENVIRONMENT

After visiting the Neurosciences Research Group at The University of Calgary, Dr. Ted Bullock, one of North America's foremost neuroscientists remarked: "This group is one of the best kept research secrets in North America."

Bullock, a distinguished professor and researcher at The University of California in San Diego, was strongly impressed with the Calgary group for the high quality of its research – quality that has been building since the late 60's when the group was established.

There are 25 researchers in the group, eight of whom are Heritage Scholars funded by the Foundation. "Heritage Funding allowed us to expand by 50 per cent. It has brought into being a significant neurosciences group in Canada", says Dr. Quentin Pittman, the group's chairman. He explains the group is now big enough and attractive enough to appeal to a high calibre of researcher. "Students are also seeking out The University of Calgary as a very desirable place to carry out (neurosciences) research."

Neuroscience is a broad and complex area where the central focus is one of the most complicated pieces of biological machinery – the brain. Within the Calgary group, the major areas of interest are: various aspects of vision, developmental neurobiology (cellular level), motor control, regulatory physiology (how the brain controls the internal body environment) and sensory mechanisms.

Left to right: Dr. Brian MacVicar, Dr. Doug Bowling, Dr. Andrew Bulloch, Dr. Fred Quandt, Dr. Phil Hicks (top), Dr. Andy Hoffer, and Dr. Rod Miller.

STUDYING THE SIGNALS

Dr. Fred Quandt, one researcher in the group, is investigating one of the most fundamental questions in neuroscience – the processes by which electrical signals are generated in neurons (nerve cells). He is using electrophysiological techniques to probe how membrane proteins in neurons generate electrical activity by responding to various stimuli.

This fundamental question is important to the understanding and treatment of diseases of the nervous system, including organic disorders such as epilepsy or dementia, congenital disorders or psychiatric disorders. By learning more about the basic properties of neurons, Quandt has been able to give clinicians more information about how anticonvulsant drugs work. "Drug companies are reading our literature to make drugs more specific and effective."

REGENERATION FOR RESTORATION

Another researcher in the neurosciences group, Dr. Andrew Bulloch, is also studying neurons, specifically regeneration.

Using the nervous system of the snail as his model (since basic biological principles apply throughout the animal kingdom) Bulloch is looking at the factors that control the growth of individual neurons. "I'm interested in comparing the ability of the adult nervous system to grow and repair itself after injury and how that capability compares to the development of the nervous system itself," he explains.

Peripheral nerves in humans (i.e. those in the hands and legs) regenerate very well, but the human central nervous system, the brain and spinal cord, shows an almost total inability to regenerate neurons. Bulloch's work, therefore, has great relevance for those suffering from paralysis caused by disease or injury.

LEARNING THE LANGUAGE

Dr. Andy Hoffer is also working in an area that has considerable importance for clinical medicine. In his research on neural control of movements he is asking: What is the language nerve cells use to communicate when controlling specific movements?

"If the language of the motor neurons is known, it becomes possible to mimic that language with electrical stimulation to treat certain cases of paralysis or other central nervous system disorders," he notes.

Hoffer is also researching electrical activity of sensory nerve fibres bringing information from the muscles to the central nervous system. This research has clinical application for controlling prostheses (an artificial device to replace a missing part of the body). A third area of Hoffer's research is the recording of the communication between the spinal cord nuclei and higher levels of the brain.

Hoffer explains: "Once scientists understand the activity patterns of nerve cells acting on muscles in healthy organisms, they will have new methods for earlier diagnosis of neurological disorders like Parkinson's disease, and new approaches to therapy."

SUPPORTING

Dr. Jonathan Tyler (centre) with his two laboratory assistants, both funded by the Foundation. David Trook (left) is a Masters student in Genetics while Dan Gietz is a Post-Doctorate Fellow in Genetics.

ALBERTA'S YOUNG SCIENTISTS

One of the most critical challenges facing medical research today is finding ways to encourage young people to pursue research careers. For bright young people to choose research, there has to be a combination of funding and the possibility of working with experienced researchers.

Until recently in Alberta, a lack of opportunities meant that aspiring scientists had to move to Eastern Canada or, more frequently, the United States to pursue their careers; or, if this was not possible, choose another career.

In the last three years new opportunities have opened up for young scientists. The Foundation is funding young people while they learn and attracting outstanding scientists to provide leadership. Researchers-in-training can receive Foundation support through three programs: Fellowships, Studentships and Summer Studentships.

According to Dr. Warren Veale, Chairman of The University of Calgary's Department of Physiology and a member of the Foundation's Scientific Advisory Council, the Foundation helps eliminate the "Catch 22" of research – no experience, no grant; no grant, no chance to gain experience.

"By providing opportunities for universities to recruit young scientists, the Foundation makes them extremely competitive for grants and funding," Veale says.

With the Foundation, he adds, worthy young investigators know that there is a career path – that they can start as a student and go on to receive support as a post-doctorate fellow.

The Dean of The University of Calgary Medical School, Dr. Mamoru Watanabe, is also keenly aware of the importance of the Foundation to young scientists.

"Our feeling is that students are attracted into research because of exposure to the right role model. They are excited and encouraged by the academic staff who are doing good research," he says.

With a Part-time Fellowship from the Foundation, Dr. Keith Jorgenson has been able to start developing a career in clinical research. Jorgenson earned his Ph.D. in biochemistry from The University of Calgary and is now working on his M.D. at that university.

With Foundation funding, Jorgenson can study medicine and at the same time develop his research skills. Without Foundation funding, Jorgenson would have had to work part-time to put himself through medical school and give up his research, which he probably could never have pursued again.

"If I had had to take years off (research) for medical school it would have been very difficult to catch up," he explains. "It's hard enough to keep up at the best of times. Research is advancing so quickly in specialized areas."

Jorgenson's ultimate aim is to carry on a clinical practice in conjunction with a research program. He feels it would be beneficial for him to gain experience in other centres, though he would like to eventually return to Alberta.

Dr. James Talbot, who earned his Ph.D. in biochemistry from The University of Alberta, also has a Foundation Part-time Fellowship to study medicine.

By supporting researchers who wish to pursue medicine the Foundation is helping to ensure that more young people stay in research.

Talbot, who is taking his M.D. at The University of Toronto, says Foundation support is invaluable for medical students with a science background. "There are applied problems in medicine that are begging for an approach that needs a basic science background," he says.

By supporting researchers who wish to pursue medicine, Talbot feels the Foundation is helping to ensure that more young people stay in research. "The fact that you've done a Ph.D. shows where your interest is."

Like Jorgenson, Talbot would eventually like to return to Alberta to pursue his career. "I like the idea of being at the beginning and helping to create and build. This is a major attraction of Alberta."

STRAIGHT TO THE HEART

Of all the diseases that afflict human beings, none has affected as many as heart disease – the number one killer.

Sudden cardiac death – that is, death without warning within an hour of the onset of symptoms – kills 4,000 people a year in Alberta alone.

At The University of Calgary, the Cardiovascular Respiratory Research Group is receiving solid support from the Alberta Heritage Foundation for Medical Research. Investigators in the group are studying various aspects of heart function with a major focus on sudden cardiac death.

"We want to be able to identify people who are prone to die suddenly before they have a problem," says Dr. George Wyse of the group.

Sudden cardiac death is by no means predictable, Wyse emphasizes, because the way in which heredity and environmental factors interact is different in each individual. As well, the importance of more controversial factors, such as stress, is still under debate.

The Cardiovascular Research Group is concentrating its efforts in two main areas – hemodynamics, the pumping function of the heart, and electrophysiology, the electrical behavior of the heart (specifically, how electrical impulses are generated and transmitted).

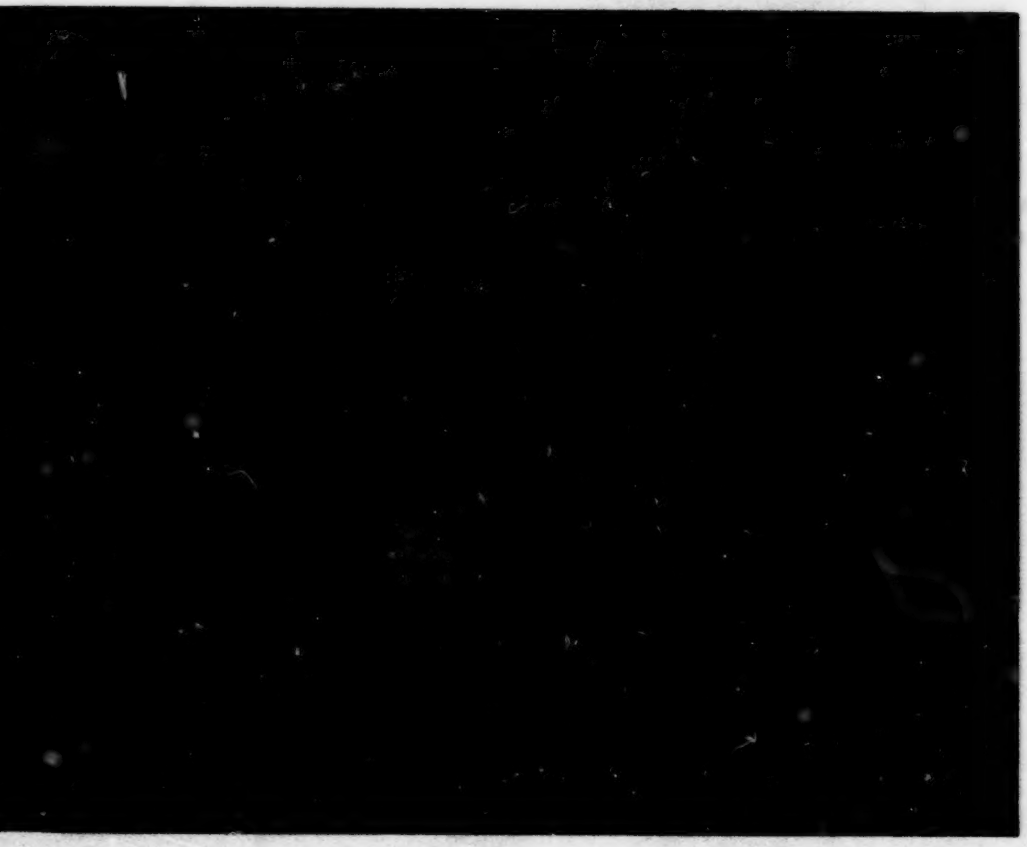
Through studies in these areas, the group is also learning more about two major methods of managing heart disease – drugs and implantable electronic devices.

New technology allows scientists to examine how specific drugs or other therapies affect heart function; conversely, by understanding the precise physiology and biochemistry of the heart they are developing new drugs and new therapies.

The Calgary group is conducting forefront studies in pharmacology, echocardiography, nuclear medicine images, angioplasty and pacemaker technology. It is one of the few heart research groups in North America which covers the spectrum from laboratory studies of single heart cells to clinical research with cardiac patients.

1 Dr. Eldon Smith prepares a patient for body surface mapping.

Electrocardiograms record the electrical activity of the heart using nine different areas in the arms and chest. Scientists have known for a long time that an increase in the number of sites on the body would yield more information, but the human mind wasn't able to integrate all the information and develop conclusions. In collaboration with Dr. M. Horacek of Dalhousie University, Dr. Eldon Smith has built a computer which allows ECG readings on 128 sites. The computer, funded by AHFMR, can record the heart's electrical activity at any given second and from these readings a contour body map can be drawn. Mapping means doctors can get information about the heart's function from the body surface, rather than using invasive techniques such as inserting catheters into the heart.



2 Heritage Scholar Dr. Henry Duff (left) and Dr. George Wyse review electrophysiologic data of a patient.

Duff is studying how various drugs affect rhythmic disturbances in the heart, known as tachycardia and ventricular fibrillation. The latter is the greatest cause of sudden death. Doctors treat these abnormalities with standard drugs like quinidine and mexiletine, but high dosages of these drugs frequently don't work and also have side effects. Duff has discovered that low dosages of both quinidine and mexiletine in combination are effective in regulating heart rhythms and have fewer side effects. If Duff can learn more about why the two drugs are therapeutically effective in combination – when each alone is not – then scientists may be able to develop even more effective drugs.

THE BODY'S IMMUNE SYSTEM

Dr. Marvin Fritzler of The University of Calgary is investigating a rheumatic disease called Systemic lupus erythematosus (SLE). The disease afflicts nearly one million North Americans, most of whom are women between 20 and 40. SLE causes inflammation and damage to organs through the body, most notably the kidneys, joints, brain and the nervous system. Blood vessels, lungs, heart and the skin may also be affected. Fritzler is investigating ways of detecting SLE at an early stage and ways to detect the reappearance of the disease once the inflammation has been brought under control. The cause of SLE is unknown, but clues to the exact cause may come from research conducted in Fritzler's laboratory.

IN FIGHTING

When it comes to fighting disease, the human body performs admirably much of the time. Our complex immune system can overcome everything from minor infections to potentially fatal ones.

At times, however, the immune system breaks down, allowing a disease agent like a virus to attack healthy cells. By learning why the immune process breaks down, researchers hope to not only learn more about disease but to synthetically reproduce the process as a preventive measure. Vaccines for diseases like polio, diptheria and mumps are strong proof of the importance of immunological research.

The Foundation supports a number of researchers working in various areas of immunology. In many of these areas, Alberta researchers are making significant progress.

TOWARDS THE PREVENTION OF MS

At The University of Alberta a team of researchers has gained international recognition by observing a relationship between the immune system and multiple sclerosis (MS). The research has particular importance for countries in the northern hemisphere, where the prevalance of MS is high. In Alberta alone, The University of Alberta's MS clinic has seen approximately 300 new patients in the last two years.

Normally, the immune system produces antibodies which combine with disease-producing agents called antigens to form immune complexes (IC). These complexes eliminate the bacteria or other foreign disease-producing agents. However, in some situations the complexes do the opposite and cause disease, such as many forms of kidney disease.

Through research, The University of Alberta team has observed that a component of human brain tissue called myelin is the constituent of immune complexes in certain MS patients. This important observation suggests that a disturbance of the body's immune system is important in the disease, rather than it being a disease only of the central nervous system.

"If this observation is validated in a large number of MS patients, it might be possible to develop a special form of treatment, possibly a vaccine," says Dr. Mrinal Dasgupta, a member of the team. He adds that by learning more about the constituent of immune complexes in patients who have the disease, he and his colleagues hope to find clues to the cause of MS.

STUDYING KILLER CELL STRENGTH

At The University of Calgary, Dr. David Matheson is also investigating the complexities of the immune system.

A pediatrician who was attracted to immunology because he feels "it is one of the fastest growing and most exciting areas of medical research", Matheson is pursuing both basic and clinical research.

In his basic research, he is studying the activity and regulation of the body's natural killer cells – cells that are thought to survey the body for malignant cells and protect it from these cells, and possibly from virus infections as well. His studies include investigating the effects of drugs on these cells.

In his clinical work, Matheson is attempting to bring knowledge gained from his basic research to his treatment of patients suffering from immune deficiency diseases.

STOPPING A VIRUS

Dr. Patrick Lee at The University of Calgary is also working in immunology at the cellular level. Lee's main interest is the relationship between the virus and a cell.

"A virus is a parasite. It cannot survive or reproduce on its own; to do so it must invade and take over a host cell," he notes. "A virus is thus very difficult to attack because its replication processes closely resemble those which function in the host cell, and any attack on the virus is often an attack on the cell itself."

Current anti-viral measures – which include vaccination and chemotherapy – have met with various degrees of success. Lee believes that another possible way to stop a virus would be to stop it before it can attach itself to a normal healthy cell. Before he develops a method to do this, he must understand how the virus attaches itself to the cell membrane in the first place.

FORM

STALKING THE KILLER CANCER

If there is one goal in medical research that has preoccupied the North American public above all others, it is undoubtedly a cure for cancer. But the much awaited cure for cancer won't occur as one sudden, giant breakthrough – it will come as a series of breakthroughs resulting from years of painstaking research.

There is still much to learn about cancer – its causes and how it progresses. One individual who is well aware of these challenges is Dr. Chris Bleackley, a researcher in the Department of Biochemistry at The University of Alberta.

"We still don't know what the basic differences are between normal cells and tumor cells," says Bleackley.

To gain a greater understanding of how cancer works, Bleackley and his colleagues are studying the immune system on a molecular level, using the tools of biochemistry and molecular genetics. The 18-member team is a good example of how various funding agencies can cooperate to support important research. Bleackley and his colleagues are funded by the Foundation, the Medical Research Council and the National Cancer Institute. In addition, Dr. Verner Paetkau is working with the assistance of a Terry Fox Initiatives Grant.

The group's studies of the immune system have considerable potential for improved therapy in the treatment of cancer and other diseases where something goes wrong with the immune system, such as AIDS, diabetes mellitus, rheumatoid arthritis and certain kidney disorders.

"KISS OF DEATH"

Bleackley is particularly interested in a molecule called Interleukin 2. This molecule is part of a group of molecules called lymphokines, which are produced by regulatory T-lymphocyte cells. Interleukin 2 is important because it stimulates the growth of killer cells which recognize a tumor cell and give it a "kiss of death", breaking open the cell. By purifying Interleukin 2 in the laboratory, Bleackley is making progress towards cloning or synthesizing the molecule for eventual application in therapy.

Bleackley finds it especially exciting that research on the immune system has such great potential for the treatment of patients. "I'm a basic researcher but it's only a short step away from clinical applications."

He notes one example of the usefulness of Interleukin 2: "Most conventional forms of therapy like chemotherapy and radiation tend to knock out the immune system. Molecules like Interleukin 2 can beef up the system after this therapy."

Dr. Chris Bleackley, a researcher at The University of Alberta, notes that scientists still don't know the differences between normal cells and tumor cells.

FIGHTING BREAST CANCER

Dr. Yvonne Lefebvre at The University of Calgary is also being supported by the Foundation (and other agencies) for cancer research. Lefebvre is investigating the use of steroid hormones in the treatment of breast cancer. Steroid hormone treatment is only successful with one-third of all known breast cancers. But it is a desirable method, Lefebvre points out, because the side effects aren't as debilitating as other methods, such as chemotherapy and radiation.

Lefebvre is studying why some breast cancers respond to steroid treatment while others don't. If, as she believes, the inability to respond is due to a defect in the cells, it may be possible to find a way to correct it.

Lefebvre hypothesizes that the cancer cells responding to hormones have special hormone-binding sites in the membrane which allow the steroids to enter the nucleus. The unresponsive cells may have some defect in the binding sites, or in the processes that take the hormones through the membranes into the nucleus.

Lefebvre's research is noteworthy because she is taking a different approach from the majority. "Most researchers working on steroids are studying how they interact with cell components within the nucleus, not how they get into the nucleus," she explains.

KEEPING THE TECHNOLOGICA

Dr. William Stell with the transmission electron microscope that The University of Calgary's Faculty of Medicine acquired with Foundation funding.

"Science almost always advances on the basis of available technology," notes Dr. George Drummond, a researcher and professor at The University of Calgary and a member of the Foundation's Scientific Advisory Council. Technological advances have revolutionized the biological sciences, he stresses, giving greater speed and efficiency. Availability of the most up-to-date equipment can be crucial to a researcher's progress.

The benefits of high technology in research are exemplified by equipment like the High Performance Liquid Chromatography (HPLC) system. This rapid and highly sensitive system can separate biological compounds, such as proteins and enzymes, in an extremely short period of time. Processes that used to take three, four and six months now take 20 minutes with the HPLC system.

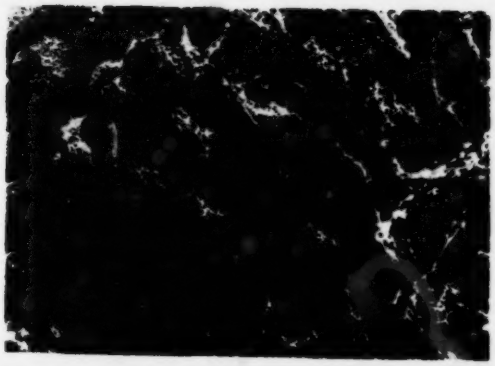
Technological advances like the HPLC system allow researchers to do more, and do it quickly, but they have made research considerably more expensive. To assist researchers the Foundation offers Major Equipment Grants as high as $350,000. These grants are supporting investigators working in a wide range of areas.

SCANNING FOR BONE DISEASE

Dr. Thomas Hangartner, a researcher in the Department of Applied Sciences in Medicine at The University of Alberta, is studying ways to treat a bone disease called osteoporosis. The disease – which leads to deterioration of the bone – is highly prevalent, particularly in post-menopausal women. Up to 50 per cent of women over 50 will have osteoporosis to a greater or lesser degree during their lifetime.

"Our research is geared to people in their senior years, since the disease usually starts to manifest itself in that period," says Hangartner.

AL EDGE



The photo at left, taken by a scanning electron microscope, is of human gall bladder mucosa (lining), showing the individual cells and mucus threads on the surface. The microscope – a delicate, high precision instrument – was purchased by The University of Alberta's Surgical Medical Research Institute with a grant from the Foundation.

Sometimes those who have the disease don't have symptoms, while others can experience backache. Current treatment methods have met with little success, which has resulted in a large cost to the health care system ($5 billion a year in the United States). "The problems encountered in diagnosing and treating bone diseases, like osteoporosis, are mainly the result of a lack of a sensitive method of measuring bone density," explains Hangartner.

With $125,000 in support from the Foundation, Hangartner and his colleagues are building a special computer tomography (CT) scanner – a machine that can give more precise measurements of bone density. Measurements from the scanner, which has no significant radiation risk, will be important in diagnosing osteoporosis in an early stage. As well, the measurements will allow the evaluation of therapeutic approaches, particularly pharmacology. With the scanner physicians can observe the immediate and long-term effects of drugs.

MEASURING MOVEMENT

At The University of Calgary Dr. Benno Nigg received a Major Equipment Grant for his research in biomechanics, the analysis of human movement. Nigg and his colleagues are quantifying load on the musculo-skeletal system, especially load that is evident in more strenuous activities such as sports. "We're concentrating on the lower extremities, including the hip, knee and ankle, and the lower back, as they are under more stress for most people," he says.

With the $260,000 grant from the Foundation, Nigg and his colleagues have purchased goniometers, which measure joint angles on-line (that is, the result is given simultaneously with the action) and accelerometers to measure acceleration. They also purchased a PDP-11/44 computer to store data on long-term tapes; another small computer is mobile for on-site research in remote locations such as hospitals.

"We want to build up a data bank with every person tested and specific information on them," Nigg explains. "That way we can ask the computer for very specific information – for example, for all the subjects with knee problems in the movement of running."

It used to take researchers days to separate biological compounds. With the High Performance Liquid Chromatography System, compounds can be separated in minutes.

"We know very little about the chlamydial organism and we can't answer questions about the long-term effects of infant infections."

PERINATAL INFECTION RESEARCHER'S CONCERN

Among venereal diseases, Chlamydia V.D. is not well-known, but it is thought to be responsible for most V.D. which isn't gonorrhea.

Dr. Wanda Wenman, a Foundation Scholar at The University of Alberta, is one of a handful of investigators in the world studying chlamydial infection. "It's probably the most common perinatal infection," she says.

Babies born to women with chlamydiae become infected during the birth process. "When they're passing through the birth canal they're literally swallowing bugs," Wenman explains. The infected infants suffer from both eye infections and pneumonia.

A conservative estimate calculates that five per cent of Canadian women carry chlamydiae, though they have no outward symptoms. Seventy per cent of the babies of these women will become infected and 10 to 20 per cent will develop pneumonia, so the problem is widespread.

"We know very little about the chlamydial organism," says Wenman, "and we can't answer questions about the long-term effects of infant infections."

She also stresses there is a need for more efficient screening. Most centres in the country aren't set up to screen mothers for chlamydiae and give antibiotics to carriers.

A University of Calgary Medical School graduate, Wenman was studying molecular biology at the University of California in Los Angeles before she returned to Alberta to take up her research. Although she is a practising pediatrician, as a Heritage Scholar Wenman is required to devote 75 per cent of her time to research. "I'm a clinician who went to basic research. A lot of times it's the other way around," she notes.

Although her specific interest is Chlamydia, Wenman feels strongly that more must be done to encourage research on infectious diseases in Canada.

BREATHING EASILY

Two Heritage Scholars focus on one of our most vital organs — the lung.

Dr. John Burka, a pharmacologist at The University of Alberta, is trying to determine whether an imbalance towards bronchoconstrictor products in the airways (as opposed to substances that dilate) contributes to asthma. He is examining the mechanisms by which the synthesis and activity of bronchoconstrictor agents, including leukotrienes and prostaglandins, can be limited to make therapy for asthma more effective.

"We're trying to develop better drugs to decrease the synthesis of compounds that cause airways to close, or block the compounds where they act (receptor sites)," Burka explains.

In the challenge to produce more selective, and consequently more efficient drugs for asthma, Burka feels researchers are making considerable progress. "Treatment for asthma will greatly improve in the next few years," he predicts.

At The University of Calgary, Dr. Gordon Ford is investigating a major but poorly understood lung problem called atelectasis (collapse of lung tissue). The disorder may arise as a result of an airway disease or may accompany a variety of other lung or chest wall (rib cage and diaphragm) disorders.

"Patients undergoing upper abdominal surgery (for example, gall bladder surgery) are particularly likely to develop characteristic changes in the way the lung functions and atelectasis," says Ford, an internist specializing in pulmonary medicine.

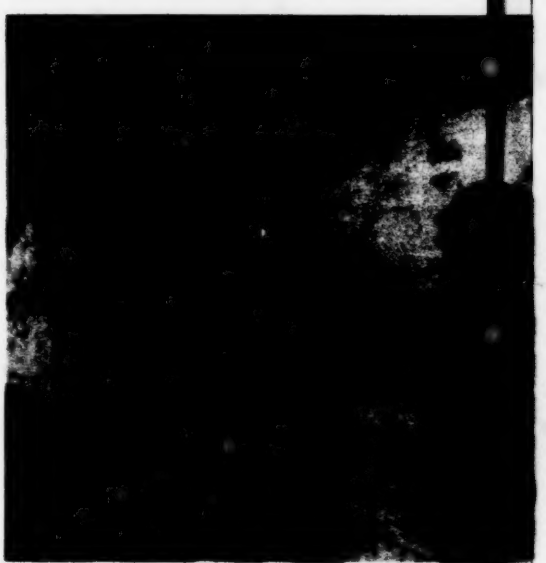
In these patients, decreased diaphragm activity has been noted during the immediate post-operative period during quiet breathing, with a return to normal activity after one to two days. Ford hopes to determine the mechanisms of this decreased activity and develop treatments aimed at decreasing or preventing its consequences in animal models. "If we find these treatments are beneficial, their principles will be applied to human patients," he says.

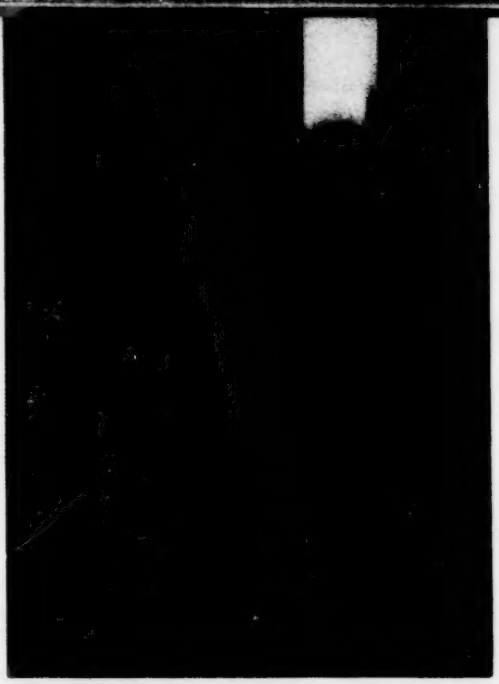
Ford is also researching the mechanisms and possible treatments for more serious forms of atelectasis, such as acute lobar atelectasis, in which one whole lung lobe collapses.

"Treatment for asthma will greatly improve in the next few years."

TOWARDS MORE EFFECTIVE DRUG THERAPY

The question of whether the metabolism of drugs can result in a beneficial or toxic effect is **Dr. Terry Danielson's** research interest. With Foundation funding, The University of Alberta researcher is studying the drug phenelzine, which is used clinically as an anti-depressant. "Structurally phenelzine is very similar to a number of compounds normally present in the brain which have mood-elevating properties," Danielson says. "We want to determine if phenelzine can be converted in the body to any of these compounds, and whether these metabolites play a role in the anti-depressant response to the drug." In addition, phenelzine has structural features in common with other chemical agents known to promote tissue damage. Danielson and his colleagues in pharmacy want to see whether the metabolism of phenelzine renders it non-toxic.

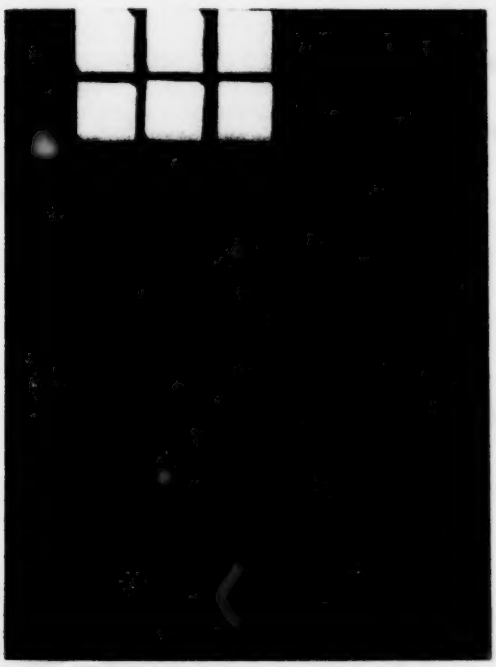


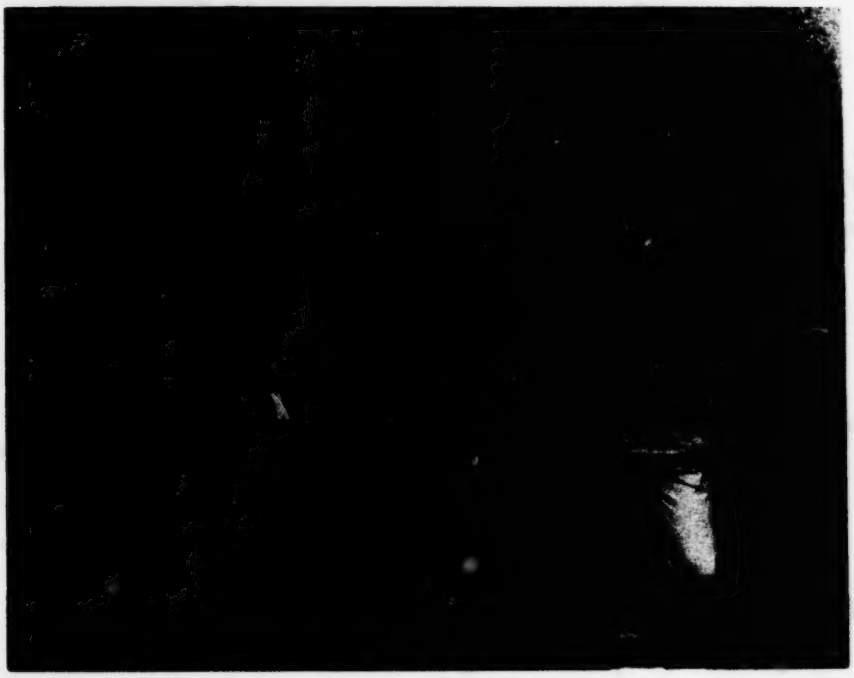


1 Dr. Terry Danielson
2 Dr. Penelope Codding
3 Dr. Diane Taylor
4 Dr. Peter Smith

Resistance to antibiotics caused by plasmids (a genetic element in a cell) has become a major problem in human and veterinary medicine. Many different kinds of plasmids exist, and new plasmids are able to evolve in response to the selection pressure imposed by antibiotics. **Dr. Diane Taylor** of The University of Alberta is working to characterize antibiotic-resistant plasmids originating in certain disease-producing bacteria. An understanding of the nature and origin of these plasmids is necessary for selecting measures to control the spread of antibiotic resistance caused by them.

Much of the management of biological processes in the body is done by chemical messages. The cells in the body send out molecules containing messages to target molecules, or receptors. Drugs often take advantage of this communication system by preventing a message from reaching its target, or sending a message stronger than the natural one. **Dr. Penelope Codding** of The University of Calgary is studying how drugs bind to receptor sites. Knowledge from her research could be used to make drugs that are more effective and have fewer side effects.





All of the electrical activity in the body's nervous system ultimately depends on an enzyme – found inside all living cells – called sodium potassium adenosine triphosphatase. With adenosine triphosphate as an energy source, a pump is created whereby sodium moves out of the cell and potassium moves in; it is this movement that is responsible for electrical activity. In his research, **Dr. Peter Smith** of The University of Alberta is studying the effects of various drugs such as steroids, neurotransmitters and anti-convulsant drugs on the enzyme. Smith's work has relevance in the treatment of epilepsy and affective disorders like depression and schizophrenia.

FOUNDATION SUPPORTS A VARIETY OF PROGRAMS

COMING . . .

Through its Visiting Scientist and Professor programs, the Foundation encourages an exchange of knowledge and skills between Alberta and other medical research centres.

"It's always a tremendous advantage to have someone from abroad," stresses Dr. Thomas Overton, Professor in the Department of Applied Sciences in Biology at The University of Alberta.

Dr. Overton's department recently benefited from the one-year visit of scientist Dr. Dan Macey, a medical physicist from The University of Oxford in England.

While he was in Alberta, Macey worked at comparing two scanning technologies for monitoring skeletal disease – whole body computed tomography for studying the axial skeleton (spine) and special purpose computed tomography for peripheral skeleton measurements (wrist).

Macey, Overton emphasizes, not only brought his considerable experience but a new perspective. "He had a completely different outlook that reflected our own introspection. We were too close to some of the problems to recognize them."

Being a visiting scientist, Macey notes, is a bit like being a troubleshooter. "It's the independence one has that's important. You can make as critical an examination as possible."

AND GOING . . .

The considerable value of studying abroad is exemplified in Dr. David Schiff's year at the Weizmann Institute of Science in Rehovot, Israel. Schiff, Director of Newborn Medicine at The University of Alberta Hospital in Edmonton, went to Israel on a Foundation Visiting Scientist Award.

In Alberta, Schiff's clinical research focused on bilirubin metabolism and lipid (fat) metabolism in the perinatal period. Working with internationally renowned researchers in Israel, Schiff learned more about lipid chemistry and basic cellular function.

The year in Israel gave Schiff the desire to spend as much time as possible conducting basic research. "I plan to apply the methods I've learned to certain problems I've been asking about the fetus and the newborn. For example, bilirubin metabolism is toxic to infants if it exceeds certain levels. I want to study what parameters of the brain cell make it more vulnerable to bilirubin toxicosis."

The study leave was also useful for Schiff's Israeli colleagues. The Alberta scientist gave his hosts valuable information for a proposed clinical study on respiratory distress syndrome of infants.

CONFERENCES

The Foundation has supported 36 national and international conferences by providing travel funds for leading scientists. The conferences have covered a range of research topics, including control of Viral Diseases, International Conference on Reproductive Immunology and Fundamental Problems of Breast Cancer.

Heritage Medical Scientist Award

This award was established to encourage the recruitment and establishment of a limited number of senior medical scientists to Alberta. A Heritage Medical Scientist is a leader in his field and is internationally recognized for the excellent quality of his scientific contributions. The successful candidate has to demonstrate an ability to develop and lead research groups and attract young people to medical science careers.

Distinguished medical scientists who are located in Alberta and whose stipend will terminate by reason of time limitations imposed by other research funding agencies are eligible. Highly successful Heritage Scholars are also eligible.

Total number of awards: 1
Expenditures: (including establishment grants) $488,200

Scholarships

Alberta Heritage Medical Research Scholarships support investigators recently trained in medical research who have demonstrated considerable promise and ability to initiate and conduct independent research. An initial award is intended to provide an opportunity to develop medical research unhampered by heavy teaching and service duties.

Scholarships are granted by competition and based upon the excellence of the candidate, the originality and importance of the project, and the quality and adequacy of the research environment into which the host institution proposes to place the candidate.

Scholars also receive establishment grants. These grants provide equipment maintenance and salaries for technicians.

Total number of awards: 49
Expenditures: (including establishment grants) $8,645,152

Independent Establishment Grants for New Investigators

A Heritage Medical Research Establishment Grant is given to a new investigator who is not funded by the Foundation (who may or may not hold a Scholarship or equivalent award from another research granting agency). This grant is designed to help new investigators quickly achieve maximal research productivity by providing equipment, technical assistance, materials and supplies.

Total number of awards: 20
Expenditures: $2,446,486

Fellowships

Heritage Medical Research Fellowships provide qualified candidates with full-time post-graduate training in research in an area of medical science relevant to the aims of the Foundation. Fellows must have an M.D., D.D.S., D.V.M., Ph.D., or equivalent degree and must demonstrate high academic standing and evidence of research ability. Awards are granted by competition based on excellence.

Total number of awards: Full-time 271
Part-time 15
Expenditures: $6,701,343

Studentships

The Foundation provides three types of awards: Full-time, Part-time, and Summer Studentships.

There are a limited number of **Full-time Studentships** for students registered in full-time M.Sc. or Ph.D. programs, and who plan careers in medical research.

The University must accept students into a graduate program and invite students to apply for an AHFMR Studentship. Studentships are granted by competition and awards are made on the basis of excellence.

A limited number of **Part-time Studentship** awards are available to full-time students working towards professional health-related degrees, and seeking to spend substantial amounts of free time in medical research. Research required by the curriculum is not eligible for support.

Summer Studentship awards support promising Alberta university students who wish to spend their summer months (May to August) engaged in medical research.

Total number of awards: Full-time 291
Part-time 29
Summer 355
Expenditures: $4,988,580

Research Allowances

(Independently Funded Students & Fellows)

Holders of full-time Studentships and Fellowships awarded by another medical research agency using similar guidelines and standards are eligible to apply to the Foundation for a Research Allowance.

Total number of awards: Studentship 63
Fellowship 43
Expenditures: $406,692

Visiting Scientists

Awards for Visiting Scientists to Alberta enable a limited number of highly innovative and productive medical scientists to engage in medical research in an Alberta university for the purpose of bringing special knowledge and expertise to the host, the department, group, or institution.

Awards for Visiting Scientists from Alberta enables Alberta medical scientists to undertake collaborative research which they are unable to undertake locally due to inadequate technology or collegial expertise. Research funded must be an obvious step in the progression of a sustained research effort on the part of the Visiting Scientist.

The program allows Alberta's active researchers to participate in new and important breakthroughs in medical research emerging elsewhere.

Total number of awards: 40
Expenditures: $733,987

Visiting Professors

Heritage Medical Research Visiting Professorships are available for the purpose of recognizing and attracting truly outstanding medical scientists to visit Alberta to enrich and enhance the climate of medical research within the universities and the affiliated institutions active in medical research.

Total number of awards: 36
Expenditures: $57,055

Alberta Heritage Medical Research Visiting Lecturers

The Visiting Lecturer program helps Alberta universities attract outstanding medical scientists who can broaden and enrich the educational experience of graduate students and fellows. The program also gives Alberta investigators, individually or in groups, the opportunity to discuss their research with others expert in their field of medical research.

Total number of awards: 563
Expenditures: $522,758

Alberta Heritage Medical Research Travel Grants

The Foundation annually gives Travel Grants to The University of Alberta and The University of Calgary to be administered by the Universities for the following purposes:

Attendance of faculty members at workshops, conferences and annual meetings.

Recruitment of researchers.

Short visits to discuss complicated experimental design and cooperative research and prepare publications stemming from cooperative research.

Short visits to other laboratories to study new research procedures and techniques and to host external investigators who can assist in the establishment of procedures and techniques.

Total number of awards: 378
Expenditures: $351,554

Professors-in-Residence

The Foundation offers a very limited number of Heritage Medical Research Professors-in-Residence Awards to provide a special opportunity for Alberta faculty members to spend one year in full-time research free of teaching and administrative responsibilities. The award is intended for the investigator whose research has achieved a point at which concentrated effort might be expected to result in unusual levels of productivity and important new knowledge. The award is not a substitute or supplement to regular university leave opportunity.

Total number of awards: 2
Expenditures: $28,176

Conference Support

The Foundation supports a limited number of conferences and workshops clearly related to the enhancement of medical research in Alberta and the transmission of significant new knowledge to those responsible for the management of patients.

Conference support is usually limited to the funding of a small number of distinguished medical scientists invited to participate as special lecturers or major participants. Funds also support a limited number of workshops on collaborative research and workshops which explore and evaluate new research fundings.

Total number of awards: 48
Expenditures: $580,911

Grants for Major Equipment

Major Equipment grants permit the University on behalf of investigators to purchase equipment essential to the conduct of high-quality research. Applications usually relate directly to research projects supported by competitive granting agencies.

Grants for Equipment Maintenance ensure adequate maintenance of major equipment wholly funded by the Foundation's Major Equipment Grants. Preferential consideration is given to expensive facilities providing support to groups of researchers and multidisciplinary projects, especially those facilities offering services to researchers with partial or full recovery arrangements for regular operating costs.

Total number of Major Equipment and Maintenance Grants: 198
Expenditures: (includes installation and maintenance) $7,905,937

The following members of the scientific communities served on the review panels advising the Foundation on the management of grant applications:

Dr. Mark Bisby, Professor, Department of Medical Physiology, Faculty of Medicine, The University of Calgary, Calgary, Alberta.

Dr. Kenneth Bowes, Professor, Department of Surgery, Faculty of Medicine, The University of Alberta, Edmonton, Alberta.

Dr. Lawrence E. Bryan, Professor, Department of Microbiology & Infectious Diseases, Faculty of Medicine, The University of Calgary.

Dr. John Colter, Professor & Chairman, Department of Biochemistry, Faculty of Medicine, The University of Alberta.

Dr. Keith E. Cooper, Vice-President – Research, The University of Calgary.

Dr. Ronald T. Coutts, Professor, Department of Pharmacy, Faculty of Pharmacy & Pharmaceutical Sciences, The University of Alberta.

Dr. George I. Drummond, Professor, Departments of Chemistry and Medical Biochemistry, Faculties of Science and Medicine, The University of Calgary.

Dr. John J. Forster, Dean, Faculty of Graduate Studies and Research, The University of Alberta. (deceased)

Dr. Grant Gall, Professor, Department of Pediatrics, Faculty of Medicine, The University of Calgary.

Dr. John A. Hargreaves, Professor, Faculty of Dentistry, The University of Alberta.

Dr. Nancy E. Henderson, Professor, Department of Biology, Faculty of Science, The University of Calgary.

Dr. Ross Hodgetts, Associate Professor, Department of Genetics, Faculty of Science, The University of Alberta.

Dr. Morley D. Hollenberg, Professor and Head, Department of Pharmacology and Therapeutics, Faculty of Medicine, The University of Calgary.

Dr. Mervin J. Huston, Dean Emeritus, Faculty of Pharmacy and Pharmaceutical Sciences, The University of Alberta.

Dr. Cyril Kay, Professor, Department of Biochemistry, Faculty of Medicine, The University of Alberta.

Dr. Keith MacCannell, Professor, Department of Pharmacology and Therapeutics, Faculty of Medicine, The University of Calgary.

Dr. E. E. McCoy, Professor and Chairman, Department of Pediatrics, Faculty of Medicine, The University of Alberta.

Dr. T. Alexander MacPherson, Assistant Dean, Scientific Affairs, Faculty of Medicine, The University of Alberta.

Dr. W. Paranchych, Professor, Department of Biochemistry, Faculty of Medicine, The University of Alberta.

Dr. Mark Poznansky, Department of Physiology, Faculty of Medicine, The University of Alberta.

Dr. Otto P. Rorstad, Assistant Professor, Department of Medicine, Faculty of Medicine, The University of Calgary.

Dr. Anthony S. Russell, Professor, Department of Medicine, Faculty of Medicine, The University of Alberta.

Dr. Royal Ruth, Professor, Department of Zoology, Faculty of Science, The University of Alberta.

Dr. E. Schaffer, Associate Professor, Department of Medicine, Faculty of Medicine, The University of Calgary.

Dr. T. Shnitka, Professor and Chairman, Department of Pathology, Faculty of Medicine, The University of Alberta.

Dr. William Stell, Department of Anatomy, Faculty of Medicine, The University of Calgary.

Dr. J. V. Tyberg, Professor, Departments of Internal Medicine & Medical Physiology, Faculty of Medicine, The University of Calgary.

Dr. David Tyrrell, Associate Professor, Departments of Biochemistry and Medicine, Faculty of Medicine, The University of Alberta.

Dr. Warren Veale, Professor & Head, Department of Medical Physiology, Faculty of Medicine, The University of Calgary.

Dr. Mamoru Watanabe, Dean, Faculty of Medicine, The University of Calgary.

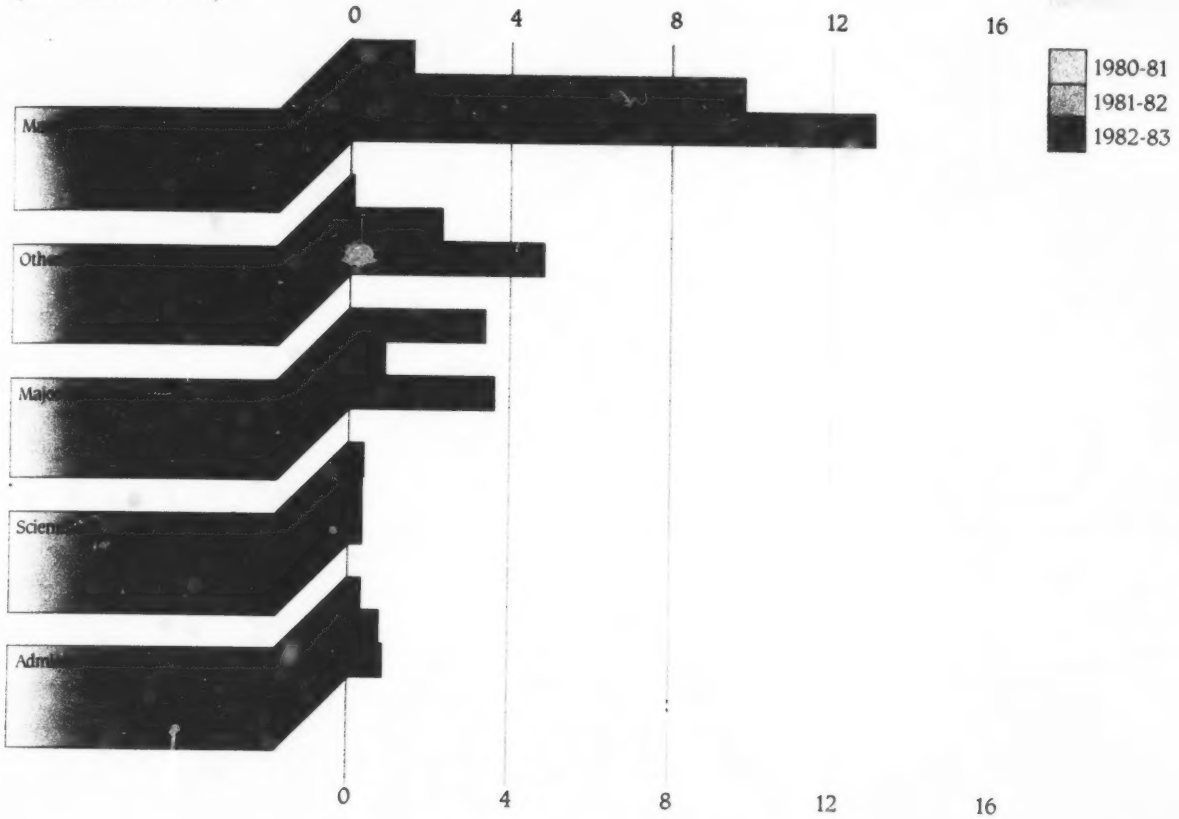
Dr. Leonard I. Wiebe, Faculty of Pharmacy & Pharmaceutical Sciences, The University of Alberta.

	1980/81	1981/82	1982/83
REVENUE	6,710,549	16,063,854	23,192,180
EXPENDITURES			
Scientific Affairs:			
Career Scientist	–	–	488,200
Scholarship & Establishment Grants	–	3,443,820	5,201,332
Independent Establishment Grants	–	1,526,338	920,148
Studentship Grants	631,107	2,083,177	2,274,296
Fellowship Grants	543,121	2,315,932	3,842,290
Independent Research Allowances	229,096	65,705	111,891
Visiting Professor	6,190	38,730	12,135
Visiting Scientist	137,322	371,616	225,049
Visiting Lecturers	50,805	152,114	319,839
Travel Grants	4,257	161,667	185,630
Conference Support	46,154	111,548	423,209
Professor In Residence	–	20,176	8,000
Major Equipment	3,339,079	910,981	3,655,877
Infrastructure Programs:			
(a) Renovations	–	666,420	2,591,938
(b) Packages*	–	150,855	131,094
(c) Cost Associated With Research	–	1,001,803	1,196,827
	4,987,131	13,020,882	21,587,755
Pre-Incorp. Recruiting and Planning	170,000	106,233	–
Administrative Expenses	372,845	784,889	814,448
Scientific Advisory Council	–	50,267	178,592
Trustee Expenses	124,589	110,823	122,168
Other Expenses	133,657	122,087	96,263
	5,788,222	14,195,181	22,799,226

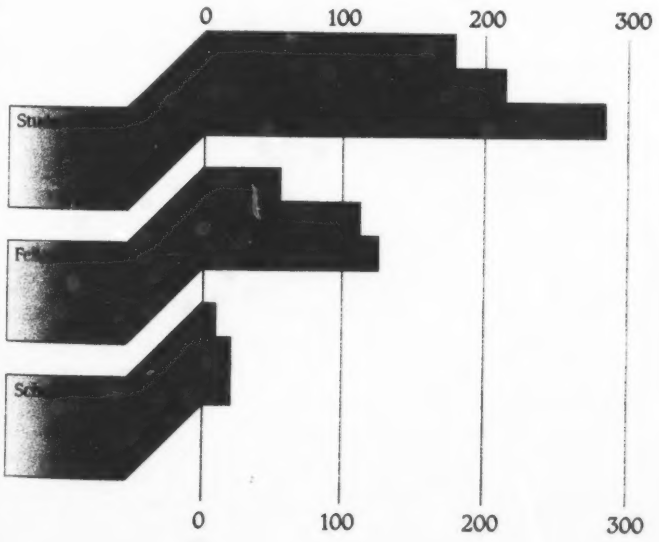
*Includes: Secretarial, Libraries, Computer, Animal Resources Recruitment and Technical Workshop

Increase of Funding 1980-83

(in millions of dollars)

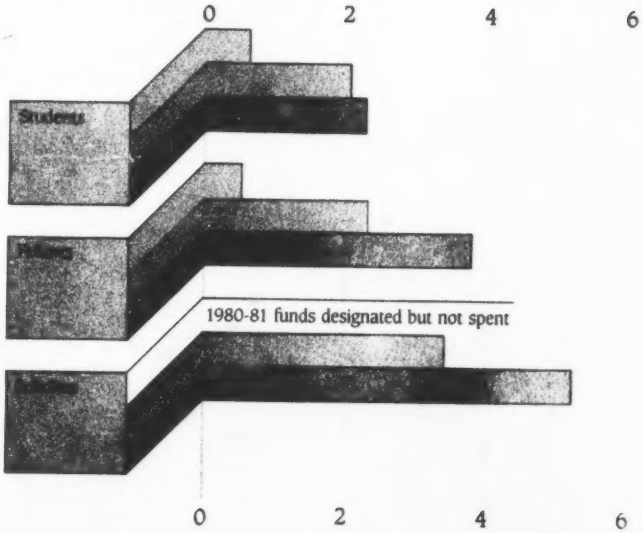


Number of Persons Funded



Amount Expended

(in millions of dollars)



GRANTS and AWARDS from April 1, 1981 to March 31, 1983
AWARD CATEGORY – IMPLEMENTED

	1980 to 1981			1981 to 1982			1982 to 1983		
	U of A	U of C	Other	U of A	U of C	Other	U of A	U of C	Other
Studentship (full-time)	56	26	1	61	32	3	69	39	4
(part-time)	5	6	0	9	4	0	3	2	0
81/04 (summer 1981)	52	25	6	–	–	–	–	–	–
82/03 (summer 1982)	–	–	–	69	33	1	–	–	–
83/02 (summer 1983)	–	–	–	–	–	–	119	43	7
Fellowship (full-time)	23	21	5	62	29	12	64	36	19
(part-time)	0	3	0	2	5	0	2	2	1
Independent Research Allowances									
Studentship	31	16	0	7	1	1	4	3	0
Fellowship	18	11	0	5	1	1	2	3	2
Scholarships	6	1	0	8	13	0	6	15	0
Independent Establishment Grants	4	4	0	3	8	0	1	0	0
Major Equipment Grants	85	26	1	62	20	0	1	2	0
Equipment Maintenance Grants	2	0	0	9	0	0	13	4	0
Conference Grants	6	7	1	14	2	0	5	11	2
Visiting Professorships	1	0	0	19	8	0	7	1	0
Professors in Residence	0	1	0	0	0	0	1	0	0
Visiting Scientists to Alberta	2	5	0	6	1	0	7	7	0
Visiting Scientists from Alberta	0	2	0	3	2	0	4	1	0
Institutional Grants	2	2	0	4	3	0	17	25	0

GRANTS and AWARDS from April 1, 1981 to March 31, 1983
AWARD CATEGORY – NUMBER OF APPLICATIONS

	1980 to 1981			1981 to 1982			1982 to 1983		
	U of A	U of C	Other	U of A	U of C	Other	U of A	U of C	Other
Studentship (full-time)	78	48	2	109	63	6	154	91	14
(part-time)	5	9	0	13	7	0	7	5	0
81/04 (summer 1981)	78	50	7	–	–	–	–	–	–
82/03 (summer 1982)	–	–	–	105	54	4	–	–	–
83/02 (summer 1983)	–	–	–	–	–	–	157	58	15
Fellowship (full-time)	38	32	8	111	47	22	136	110	53
(part-time)	0	3	0	4	6	0	4	5	1
Independent Research Allowances									
Studentship	32	16	0	7	1	1	6	6	1
Fellowship	21	14	0	6	1	1	5	8	8
Scholarships	9	10	2	22	22	0	21	25	0
Independent Establishment Grants	7	10	0	12	9	0	5	0	1
Major Equipment Grants	134	33	1	89	26	0	5	2	0
Equipment Maintenance Grants	2	0	0	16	2	0	13	6	0
Conference Grants	12	9	2	17	4	0	10	14	2
Visiting Professorships	1	0	1	29	10	1	9	2	0
Professors in Residence	1	1	0	2	0	0	2	0	0
Visiting Scientists to Alberta	5	7	0	13	7	0	21	13	0
Visiting Scientists from Alberta	0	5	0	7	6	0	9	3	2
Institutional Grants	2	2	0	4	3	0	17	25	0

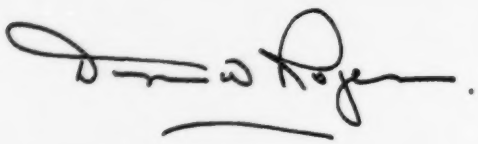
Alberta Legislature
Office of the Auditor General

AUDITOR'S REPORT

To the Trustees of the Alberta Heritage Foundation For Medical Research

I have examined the balance sheet of the Alberta Heritage Foundation for Medical Research as at March 31, 1983 and the statements of revenue and expenditure and revenue surplus for the year then ended. My examination was made in accordance with generally accepted auditing standards, and accordingly included such tests and other procedures as I considered necessary in the circumstances.

In my opinion, these financial statements present fairly the financial position of the Foundation as at March 31, 1983 and the results of its operations for the year then ended in accordance with generally accepted accounting principles applied on a basis consistent with that of the preceding year.



Douglas W. Rogers,
C.A.
Auditor General

Edmonton, Alberta
October 11, 1983

STATEMENT A

BALANCE SHEET as at MARCH 31, 1983

	1983	1982
ASSETS		
Deposits in trust (Note 3)	$ 3,239,044	$ 1,783,750
Accounts receivable (Note 4)	113,184	967,823
Accrued interest receivable	59,197	360,876
Prepaid expenses	3,455	1,772
Deposits on purchase of fixed assets	–	913
Mortgages receivable (Note 5)	259,654	–
Fixed assets, at cost less accumulated depreciation and amortization	241,847	264,099
	$ 3,916,381	$ 3,379,233
LIABILITIES AND SURPLUS		
Accounts payable	$ 665,451	$ 521,257
Revenue surplus, Statement C	3,250,930	2,857,976
	$ 3,916,381	$ 3,379,233

The accompanying notes are part of these financial statements.

STATEMENT OF REVENUE AND EXPENDITURE
for the year ended MARCH 31, 1983

STATEMENT B

	1983	1982
REVENUE		
Transfers from the Alberta Heritage Foundation for Medical Research Endowment Fund	$22,000,000	$15,000,000
Interest	1,192,180	1,063,854
	23,192,180	16,063,854
EXPENDITURE		
Scientific affairs:		
Scholarship and establishment grants	5,201,332	3,443,820
Fellowship grants and research allowances	3,842,290	2,315,932
Major equipment and maintenance grants	3,655,877	910,981
Institutional grants	2,705,280	817,275
Studentship grants and research allowances	2,274,296	2,083,177
Research support costs	1,196,827	1,001,803
Independent establishment grants	920,148	1,526,338
Heritage career scientist grants	488,200	–
Conference support grants	423,209	111,548
Visiting lecturer grants to universities	319,839	152,114
Visiting scientist grants	225,049	371,616
Travel grants to universities	185,630	161,667
Independent research allowances	111,891	65,705
Recruitment and planning grants to universities	17,752	106,233
Visiting professor honoraria and travel grants	12,135	38,730
Research professor-in-residence	8,000	20,176
	21,587,755	13,127,115
Administration expenses, Schedule 1	814,448	784,889
Scientific Advisory Council expenses	178,592	50,915
Trustee expenses	122,168	110,823
Other committee expenses	96,263	121,439
	22,799,226	14,195,181
Operating surplus for the year	$ 392,954	$ 1,868,673

STATEMENT OF REVENUE SURPLUS
for the year ended MARCH 31, 1983

STATEMENT C

	1983	1982
Revenue surplus at beginning of year	$ 2,857,976	$ 911,851
Operating surplus for the year, Statement B	392,954	1,868,673
Refund of prior year's major equipment grants	–	245,075
Research support costs applicable to prior year	–	(167,623)
Revenue surplus at end of year	$ 3,250,930	$ 2,857,976

NOTES TO THE FINANCIAL STATEMENTS MARCH 31, 1983

NOTE 1

Authority

The Alberta Heritage Foundation for Medical Research operates under the authority of the Alberta Heritage Foundation for Medical Research Act, Chapter A-26, Revised Statutes of Alberta 1980.

NOTE 2

Significant Accounting Policies and Reporting Practices

(a) Transfers from the Alberta Heritage Foundation for Medical Research Endowment Fund:

Section 8 of the Act provides that money required by the Foundation shall be paid from a $300,000,000 Endowment Fund at the request of the Foundation. The Act also provides that payments shall not be made if they would result in the cost value of Endowment Fund assets being less than $300,000,000. On this basis, the total available for transfer to the Foundation as at March 31, 1983 amounted to approximately $100,000,000.

(b) Depreciation and Amortization:

Furniture and equipment is depreciated on a straight line basis at the rate of 10% per annum to a maximum of 90% of cost. Leasehold improvements are amortized on a straight line basis over the term of the lease.

(c) Changes in Financial Position

A statement of changes in financial position is not provided as disclosure in these financial statements is considered to be adequate.

NOTE 3

Deposits in Trust

Deposits in trust consist of deposits in the Consolidated Cash Investment Trust Fund of the Province of Alberta.

NOTE 4

Accounts Receivable

Accounts receivable consist of the following:

	1983	1982
Unexpended grants held by universities:		
Travel	$ 74,445	$230,075
Visiting lecturer	11,047	97,886
Recruitment and planning	9,892	23,766
Equipment	–	592,020
Miscellaneous	17,800	24,076
	$113,184	$967,823

NOTE 5

Mortgages Receivable

Mortgages receivable represents the unpaid principal on mortgage advances to research scientists.

NOTE 6

Commitments

As at March 31, 1983 the Foundation had committed the following amounts for scientific affairs expenditure:

Scholarship and establishment grants	$ 9,099,054
Fellowship grants and research allowances	1,854,294
Major equipment and maintenance grants	1,745,170
Institutional grants	763,776
Studentship grants and research allowances	758,159
Heritage career scientist grants	688,500
Visiting lecturer grants	345,000
Independent establishment grants	250,142
Travel grants	195,000
Visiting scientist grants	128,737
Conference support grants	21,000
Research professor-in-residence	8,000
Visiting professor honoraria and travel grants	6,879
Independent research allowances	2,500
	$15,866,211

NOTE 7

Comparative Figures

The 1982 figures have been restated where necessary to conform to 1983 presentation.

NOTE 8

Approval of Financial Statements

These financial statements were reviewed by the Audit Committee on October 11, 1983 and recommended for approval by the Trustees.

SCHEDULE OF ADMINISTRATION EXPENSES
for the year ended MARCH 31, 1983

SCHEDULE 1

	1983	1982
Salaries	$435,713	$331,383
Rental of premises	100,193	89,292
Depreciation and amortization	45,976	44,245
Stationery, printing and office supplies	44,904	39,368
Employee benefits	43,714	31,476
Consultants fees	30,325	88,969
Public relations and advertising	29,217	23,230
Travelling and accommodation	19,938	35,046
Vehicle	19,355	16,298
Maintenance	9,163	5,166
Telephone	8,127	7,468
Accounting and legal fees	6,876	5,138
Insurance	6,505	5,700
Recruitment	5,496	39,805
Postage and courier	5,168	2,962
Equipment rental	2,576	6,452
Purchased services	–	6,962
Miscellaneous	1,202	5,929
	$814,448	$784,889

AHFMR HERITAGE MEDICAL SCIENTIST AWARD

WANG, Jerry H., Ph.D.
Professor, Department of Medical Biochemistry
Faculty of Medicine, The University of Calgary

Date of Appointment: 82/12/01

STUDIES IN CELL REGULATION

Living cells rely on an intracellular communication system to adjust cellular activities during changes in external environment. The basic elements of this system are certain small molecules known as second messengers whose cellular concentration can be readily changed by disturbance from outside and whose function is to modulate various cellular processes. There are two general and universal second messengers: Ca2 + and cyclic AMP. The metabolisms and actions of these two messengers are interrelated by a host of enzymes and protein factors. The long term objective of this proposal is to elucidate the principles underlying the complex interactions in the communication system.

One of the major approaches is to select key enzymes and proteins for the study of their regulatory properties, and their interactions with other components of the system. The present focus is on a Ca2 + binding protein, calmodulin, which has been implicated in various cellular processes by regulating key enzymes or proteins in these processes. To elucidate the general mechanism of the action of calmodulin, the cyclic nucleotide phosphodiesterase is selected for detailed kinetic and thermo-dynamic study of its activation process. To investigate evolutionary and functional relationships among calmodulin-dependent proteins, as well as structure-function relationships of selected enzymes, monoclonal antibodies will be developed as structure and function probes. Calmodulin-dependent protein kinases will be studied to explore the complexity of the calmodulin regulatory system. A calmodulin-dependent phosphatase will be studied in terms of its physiological significance. The protein kinases and phosphatase are selected for studies because they are expected to interact with many other proteins in the communication systems in the cells.

Another major approach is to use cultured cells to study calmodulin and calmodulin-dependent proteins under various culture conditions. These studies will illustrate how calmodulin functions in living cells and how calmodulin and its regulated protein may be controlled under different physiological conditions. The Cell Regulation Unit has obtained evidence to suggest calmodulin may function in controlling the phosphorylation states of tyrosine. The phosphorylation of protein tyrosyl residue has been implicated recently in the modulation of cell growth. Another finding is that cAMP phosphodiesterase, an enzyme which is involved in the metabolism of cAMP, a second messenger, exists as different isozymes in mammalian brain. This observation may lead to a better understanding of how the two major second messenger systems, Ca2 + and cAMP systems, are inter-linked.

AHFMR SCHOLARSHIP AWARDS

ANDERSON, Maurice J., Ph.D.
Assistant Professor,
Department of Pharmacology & Therapeutics,
Faculty of Medicine, The University of Calgary

Date of Appointment: 83/01/04

DEVELOPMENT OF NEUROMUSCULAR JUNCTION

This is a molecular study of the synaptic apparatus joining nerves and skeletal muscles. During embryonic development, growing nerves make contact with skeletal muscle cells and this generates specialized cellular structures at the forming motor endplace. This poorly understood "trophic" or "inductive" interaction appears to also contribute to the maintenance of neuromuscular apparatus in adults. Degenerative diseases such as muscular dystrophy may involve lesions in these mechanisms.

Anderson uses monoclonal antibodies as probes to study the molecular structure of the neuromuscular junctions and also observes their formation in cell cultures.

ALLEN, Peter S., Ph.D.
Professor,
Department of Applied Sciences in Medicine,
Faculty of Medicine, The University of Alberta

Date of Appointment: 83/01/01

THE IMAGING AND BIOCHEMICAL APPLICATIONS OF NMR TO MEDICINE

This is a study of the application of nuclear magnetic resonance (NMR) to body imaging and spectroscopy. NMR imaging provides cross-sectional internal pictures which display the anatomy in a way that emphasizes regions of abnormality and disease. Spectroscopy monitors body function by, for example, measuring the concentrations of certain important biochemicals relevant to various disease states. Both NMR capabilities have great potential for detecting and evaluating the results of the treatment.

In the first stage, this research involves only animal models to be followed by stage II, clinical studies on people. The projects are jointly funded by the Alberta Heritage Foundation for Medical Research and the Alberta Heritage Applied Cancer Program through the Alberta Cancer Board.

BENTLEY, Michael M., Ph.D.
Research Associate, Department of Biology,
Faculty of Science, The University of Calgary

Date of Appointment: 82/01/01
End of Appointment: 82/08/31

MOLYBDO-ENZYMES IN THE DROSOPHILA MODEL SYSTEM

This was a study of complex gene interactions involved in the production of molybdo-enzymes. Bentley uses the fruit fly for a research model because there are a large number of known mutants which affect four molybdenum enzymes and others can be readily generated. Bentley investigated how various genes interact to allow the organism to express these enzymes and modulate their levels.

Alterations of these enzymes in humans are related to certain diseases and understanding the biological processes may eventually lead to new methods for controlling genetic diseases.

Bentley accepted a tenure-track position at The University of Calgary, but continues to receive an AHFMR Establishment Grant.

BIDDLE, Fred G.
Assistant Professor, Department of Pediatrics
Faculty of Medicine, The University of Calgary

Date of Appointment: 81/09/01

GENETIC STUDIES OF THRESHOLD TRAITS OF MAMMALIAN DEVELOPMENT

This is a study of birth defects which are genetically determined and are labelled "threshold traits" because not all individuals with a genetic disposition to express the defect do so. Cleft lip and spina bifida are examples of threshold traits. Using mouse embryos, Biddle is investigating the interaction between the genetic information, its control of developmental processes and variable environmental "insults" or factors.

He is also studying the cellular processes that regulate the normal segregation of the sex chromosomes (X and Y) in spermatocytes, again using the mouse model which includes a series of inherited mutations with birth defects. Since similar birth defects occur in man, these studies on genetic and environmental factors will increase our understanding of the probability of producing abnormal sperm.

BOISVERT, Donald, M.D., Ph.D.
Associate Research Professor,
Department of Surgery,
Faculty of Medicine, The University of Alberta

Date of Appointment: 81/01/01

PATHOPHYSIOLOGY AND THERAPY OF CEREBROVASCULAR OCCLUSION

This is a study of brain damage following occlusion of a cerebral artery, commonly known as a stroke. While scientists know some irreparable brain damage occurs minutes after a stroke, recent investigations indicate variable amounts of brain tissue survive for hours or days in a "live" but non functional state. The length of survival depends upon the severity and duration of the decrease in blood supply. Boisvert is identifying the factors which determine the level of residual blood flow during initial hours after the stroke occurs.

This study may lead to the development of emergency treatment strategies to minimize the destruction of brain cells in stroke patients.

BOURNE, Gregory A., M.D.
Assistant Professor, Department of Physiology
Faculty of Medicine, The University of Alberta

Date of Appointment: 82/10/28

THE REGULATION OF TESTICULAR GnRH RECEPTORS AND GnRH-LIKE PEPTIDES AND THEIR ROLES IN STEROIDOGENESIS

This is a study of inter-related hormones which regulate gonadal function, particularly a newly identified compound localized in the ovaries and testes. This new compound seems to function like GnRH, a peptide produced in the hypothalmus known to regulate production of eggs and ovulation in females and production of testosterone and sperm in males. The GnRH-like compound also appears to control sexual maturation and senescence.

Bourne's research may provide the molecular basis for the development of new drugs such as a male contraceptive, a treatment for precocious puberty, a treatment for decreased gonadal function in old age.

BOWLING, Douglas, Ph.D.
Assistant Professor,
Department of Medical Physiology,
Faculty of Medicine, The University of Calgary

Date of Appointment: 82/09/14

PROJECTIONS OF SINGLE IDENTIFIED RETINAL AXONS

This is a study of the long axons, extensions of nerve cells in the retina which relay visual signals from the eye to the brain. After transmission via the axons, the brain processes the signals of color, form, brightness and movement. This project is designed to discover how information is encoded for transmission, how the axon connections are distributed at sites of termination in the brain, and how the connections are formed during development.

Though this research is clearly relevant to fundamental questions regarding vision, it is also more generally applicable to other questions in neurological medicine.

BULLOCH, Andrew, Ph.D.
Assistant Professor,
Department of Medical Physiology,
Faculty of Medicine, The University of Calgary

Date of Appointment: 82/07/01

CELLULAR BASIS OF ADULT NEURONAL PLASTICITY

This is a study of the capabilities of the adult nervous system to grow and adapt to change. This involves combined electrophysiological and morphological study of adult molluscan neurons as they exhibit neurite outgrowth and synapse formation. Neurons are examined both within the normal environment of ganglia in organ culture and also as dissociated cell cultures. Additionally, neurite outgrowth can be invoked *in situ* by various manipulations involving trauma to the animal, but not directly damaging the nervous system. The goal of such studies is to determine the factors which can evoke growth and determine the specificity of synapses in the adult nervous system. This information is relevant to the treatment of injuries, paralysis and other disease states where nerves are damaged.

BURKA, John F., M.D.
Assistant Professor, Department of Pharmacology,
Faculty of Medicine, The University of Alberta

Date of Appointment: 81/08/01

THE ROLE OF AA METABOLITES IN AIRWAYS HYPERREACTIVITY

This is a study of products of arachidonic acid (AA) which contribute to the tone of bronchial airway smooth muscle. In disease states such as asthma, there is increased synthesis and activity of broncho-constrictor agents. Burka is identifying the products of AA, determining their effect on airways physiology, and exploring mechanisms which could limit their activity. This study may lead to improved treatments for asthma.

Burka is also investigating two other diseases: gall bladder disease (role of AA metabolites) and rheumatoid arthritis (synovial fluid and leukocytes).

CARNE, Thomas, Ph.D.
Assistant Professor, University Biochemistry Group
Departments of Medicine and Science,
The University of Calgary

Date of Appointment: 81/09/01

BIOSYNTHESIS OF PITUITARY HORMONES

This is a study of enzymes in the pituitary gland which synthesize three peptides from a common precursor. These hormones control many aspects of the body's metabolism including synthesis of steroids, mobilization of lipid from the liver and adipose tissue, and salt and water reabsorption. Carne is identifying the products formed by reacting the enzymes with precursors synthesized from messenger RNA *in vitro*. He also works with synthetic peptides.

This research may lead to the development of new drugs which inhibit specific hormonal production and can be used to treat disorders such as Cushing's Syndrome where there is an excess of one pituitary hormone.

CODDING, Penelope, Ph.D.
Assistant Professor, Department of Chemistry,
Faculty of Science, The University of Calgary

Date of Appointment: 81/07/01

MOLECULAR STRUCTURE/FUNCTION STUDIES OF CNS ACTIVE DRUGS AND TOXINS

This is a study of how drugs bind to target molecules and thereby change their shape and their biochemistry. The drug molecule interaction depends upon the shapes of both drug and receptor molecules and their three-dimensional distribution of reactive groups. Codding uses X-ray diffraction to identify the three-dimensional shapes of drugs which have similar pharmacological effects and similar targets. This information is helpful in the development of new, more effective drugs that are specific for one target. Codding hopes to identify structural requirements for the binding of anti-anxiety drugs.

She also has developed a research model of the sodium channel receptor site for toxins. Toxins send messages to nerve and muscle cells and cause aberrant electrical properties, for example, in seizures or heart misfirings. The model defines the structure necessary for effective binding and may lead to more information about the receptor and about ion transport. She also analyzes synthesized DNA complexed with several anti-cancer drugs. These structures will show how the drug binds DNA and influences DNA biochemistry.

DANIELSON, Terry, Ph.D.
Assistant Professor,
Faculty of Pharmacy & Pharmaceutical Sciences,
The University of Alberta

Date of Appointment: 81/07/01

METABOLISM AND PLASMA LEVELS OF CLINICAL MONOAMINE OXIDASE INHIBITORS

This is a study of monoxidase inhibitors, drugs used to manage psychiatric illnesses. Though drugs like phenelzine appear to benefit patients, scientists don't know why nor do they understand why often 10 to 14 days of treatment are required before any improvement appears. Danielson is investigating how the body handles phenelzine after acute or chronic dosing by measuring drug levels in animal tissue and in the plasma or urine of psychiatric patients. Differences will be related to the development of antidepressant or toxic responses.

Danielson is also using animal models to investigate new psycho-active substances.

DASGUPTA, Mrinal K., M.D.
Assistant Professor,
Department of Medicine,
Faculty of Medicine, The University of Alberta

Date of Appointment: 82/07/01

MBP SPECIFIC CIC IN MULTIPLE SCLEROSIS

This is a study to establish biological assays to detect immune complexes (IC) in the blood and their relationship to disorders such as lupus, cystic fibrosis and multiple sclerosis (MS). In these autoimmune diseases, the immune complexes (protein antibodies plus disease-producing agents) seem to cause disease rather than fight it. Dasgupta has discovered IC level is important in multiple sclerosis patients. These IC's contain a protein found in the "myelin" covering of nerve fibres and degradation of this myelin causes the crippling symptoms.

Dasgupta is further investigating specific "myelin" in the IC's of large numbers of MS patients to see if the IC's could modulate the clinical expression of symptoms. This may lead to new forms of therapy and possibly a vaccine. The same techniques in IC research are also being applied to a form of kidney disease and cystic fibrosis.

DAVISON, Joseph, Ph.D.
Professor, Department of Medical Physiology,
Faculty of Medicine, The University of Calgary

Date of Appointment: 82/07/29

NERVOUS CONTROL OF GASTROINTESTINAL SECRETION AND MOTILITY

This is a study of nervous control of pancreatic, salivary and gastric secretions and the neurophysiology of gastrointestinal reflexes. Davison uses a multidisciplinary approach to study three aspects of secretion: The function of transmitters at the cellular level, the electrophysiological events associated with glandular secretion, and the physiological role of several apparent transmitters.

In the second thrust of his research, Davison is investigating how spontaneous gastrointestinal movement is controlled by vagovagal reflexes and peripheral sympathetic reflexes.

Because gastrointestinal secretions and movements are critical to many body processes, this basic research on normal function will lead eventually to greater understanding of many disease states.

DUFF, Henry J., M.D.
Assistant Professor, Department of Medicine,
Faculty of Medicine, The University of Calgary

Date of Appointment: 82/07/01

MECHANISTIC APPROACH TO ANTIARRHYTHMIC THERAPY

This is a study of the mechanisms of drug action for drugs used to treat cardiac diseases. Duff evaluates known drugs, develops new ones, and uses drugs as probes to further understand the basic physiology of the heart. In animal and clinical studies, he particularly investigates antiarrhythmic drugs like quinidine and mexeletine, which are used to control irregular heart rhythms.

In more basic studies, he explores the electrophysiologic changes caused by drugs. This includes a search for specific receptors on heart cell membranes, knowledge which would lead to improved specifically-targeted drugs with less side effects.

FORD, Gordon, M.D.
Assistant Professor,
Department of Internal Medicine,
Faculty of Medicine, The University of Calgary

Date of Appointment: 82/07/01

INTERDEPENDENCE OF THE LUNG, RIBCAGE AND DIAPHRAGM DURING ATELECTASIS

This is a study of atelectasis, (areas of lung collapse) which arises from airway disease or accompanying other lung disorders. Atelectasis is particularly common in patients who have had upper abdominal surgery. Ford is investigating the cause of postoperative diaphragm dysfunction and developing experimental therapies.

Once the physiological mechanism is understood and test therapies have proved beneficial, they will be applied to clinical studies for the treatment and possible prevention of atelectasis.

FRITZLER, Marvin J., M.D., Ph.D.
Associate Professor,
Department of Internal Medicine,
Faculty of Medicine, The University of Calgary

Date of Appointment: 82/07/01

ANTINUCLEAR ANTIBODIES: AUTOIMMUNE DISEASES

This is a study of antinuclear antibodies in the serum of patients with autoimmune diseases (diseases where the immune system breaks down and seems to cause disease rather than fight it). Scientists don't understand why unusual antibodies coincide with certain diseases. Fritzler is screening the blood of thousands of donors and follows patients to see if the antibodies are precursors of the disease. He is also using biochemistry techniques to isolate, purify and characterize corresponding nuclear antigens (substances capable of inducing the formation of antibodies).

GORDON, Tessa, Ph.D.
Associate Professor, Department of Pharmacology,
Faculty of Medicine, The University of Alberta

Date of Appointment: 81/01/01
End of Appointment: 82/12/31

TROPIC INTERACTION BETWEEN NERVE AND MUSCLE

This was a study of the interdependence of peripheral motor nerves and skeletal muscle fibres. In animal models of clinical nerve injury, Gordon investigated the extent of recovery following surgical repair of injured nerves. This study will increase understanding of their trophic interaction between cells in the nervous system and the processes underlying degeneration and regeneration. Such information may eventually lead to improved therapies for patients with injuries or degenerative nerve diseases.

Tessa Gordon is now being funded by the Medical Research Council of Canada.

HANGARTNER, Thomas, Ph.D.
Associate Professor,
Department of Applied Sciences in Medicine
Faculty of Medicine, The University of Alberta

Date of Appointment: 81/01/01

DUAL ROTATION COMPUTED TOMOGRAPHY SYSTEM FOR BONE AND TISSUE DENSITOMETRY

This is a study of bone disease made possible with a special computed tomography scanner which measures bone density. The scanner enables Hangartner to observe growth and maintenance patterns in the human skeleton. He can determine how bones are affected by hormones, diet, exercise, drugs and other treatments. He is comparing the efficacy of various treatments and has, for instance, found that intermittant drug therapy seems more effective than the traditional prolonged drug intake.

HANLEY, David A., M.D.
Assistant Professor, Department of Medicine,
Faculty of Medicine, The University of Calgary

Date of Appointment: 81/04/01

PARATHYROID HORMONE (PTH) SECRETION

This is a study of the mediators of parathyroid hormone secretion. PTH is the main regulator of calcium metabolism, a process which is important to normal cell function in all body tissues. This study uses normal animal tissue and abnormal human tissue from parathyroid disease patients.

Abnormalities of parathyroid function have been noted in many common disease states: kidney stones, chronic renal failure, generalized bone disease such as osteoporosis, and benign tumors of parathyroid glands.

HICKS, T. Philip, Ph.D.
Assistant Professor,
Department of Medical Physiology,
Faculty of Medicine, The University of Calgary

Date of Appointment: 81/09/01

IDENTIFICATION OF SYNAPTIC TRANSMITTERS IN THE MAMMALIAN VISUAL SYSTEM

This is a study of how visually responsive neurons in the brain communicate via chemical transmitters. Hicks is investigating the chemical mediators, particularly amino acids, to determine their role in processing visual information. He hypothesizes that different portions of the visual pathway which are anatomically segregated and have different functions are also separated by the use of different synaptic transmitters. His investigations are carried out at the level of the single cell using neurochemical, pharmacological and physiological techniques on animal models.

HINDSGAUL, Ole, Ph.D.
Assistant Professor,
Department of Chemistry, The University of Alberta

Date of Appointment: 81/10/01

BIOLOGICAL RECOGNITION OF COMPLEX CARBOHYDRATES

This is a study of how protein receptor-sites specifically recognize complex carbohydrates. The recognition process is a primary step in many body functions such as hormonal regulation, immunological processes and cell recognition and adhesions. Hindsgaul is looking for the molecular description of how the carbohydrates are recognized. He believes the surface of complex sugars contain discreet, predictable topographical features.

This basic research will lead to more understanding of how the mechanism mediates normal and abnormal body functioning.

HOAR, David I., Ph.D.
Associate Professor,
Department of Medical Biochemistry
Faculty of Medicine, The University of Calgary

Date of Appointment: 81/09/01

DNA SEQUENCE DIVERSITY IN MAN

This is a study of DNA sequence changes in relation to specific inherited diseases. Alterations in DNA sequences appear to be caused by mechanisms apparently similar to the function of RNA tumor viruses. Of the several thousand genetically-inherited diseases very few have been characterized (the molecular structure identified), to sufficiently identify the basic defect. New molecular biology and recombinant DNA techniques now allow Hoar to identify DNA sequence changes with specific diseases. If he can establish linkage associations, the information could be used for diagnostic studies. In the future, physicians may be able to precisely predict who will inherit certain diseases, an important step towards prevention.

HOFFER, Andy, Ph.D.
Assistant Professor,
Departments of Medical Physiology and
Clinical Neurosciences
Faculty of Medicine, The University of Calgary

Date of Appointment: 82/11/05

NEURAL CONTROL OF MOVEMENTS

This is a study of how neural function controls muscle contraction leading to voluntary movement. Hoffer records electrical currents in single, specifically-identified nerve cells in the spinal cord during normal animal movement. This is possible because of recently developed recording devices which are surgically implanted in animals. Hoffer is studying three aspects: the "language" of motor neurons, the electrical activity of sensory nerve fibres bringing information from the muscles to the motor neurons, and the communication between the spinal cord segments and higher levels of the brain.

Hoffer's implantable interfaces with nerve and muscle have recently found clinical application in the control of prosthetic limbs in amputees. This research is also very relevant to the development of new therapies and diagnostic procedures for neurological disorders like Parkinson's Disease.

IATROU, Kostas, Ph.D.
Assistant Professor,
Department of Medical Biochemistry,
Faculty of Medicine, The University of Calgary

Date of Appointment: 81/07/01

THE CHORION OF BOMBYX MORI AS A MODEL SYSTEM FOR THE STUDY OF THE ORGANIZATION, EXPRESSION AND EVOLUTION OF EUKARYOTIC MULTIGENE FAMILIES

This is a study of mechanisms regulating differential gene expression which results in normal or abnormal cellular differentiation and development. The chorion (eggshell) of the silkmoth is used as a model system because it is composed of many distinct proteins encoded by a large number of genes whose expression is developmentally regulated according to a strict temporal program. Wild type and mutant silkmoth strains are used for the analysis of the molecular organization of chorion genes expressed at different stages of oogenesis. Iatrou is identifying elements that may be involved in the control of chorion gene activation, and testing regulatory models of differential gene activity.

Understanding gene regulation at the molecular level may lead to more understanding of abnormal cellular behaviour and eventual treatment for disorders of cell differentiation and development, among which genetic defects and cancer are paramount.

JARVIS, Simon, Ph.D.
Assistant Professor, Department of Physiology,
Faculty of Medicine, The University of Alberta

Date of Appointment: 82/08/01

MOLECULAR PROPERTIES AND REGULATION OF THE NUCLEOSIDE TRANSPORT SYSTEM

This is a study of nucleosides, agents used in the treatment of viral and neoplastic diseases. Because the agents (nucleoside analogs) enter cells through a saturable transport mechanism in the cell membrane, the transportability of an analog is an important determinant of cytotoxicity. Jarvis is investigating the molecular basis of nucleoside transport using a high-affinity nucleoside transport inhibitor. Once the membrane components are identified, he will examine the regulation and synthesis of nucleoside transport protein.

This study has direct relevance to viral and cancer chemotherapy.

JENSEN, Susan, Ph.D.
Assistant Professor, Department of Microbiology
Faculty of Science, The University of Alberta

Date of Appointment: 81/07/01

BIOSYNTHESIS OF NOVEL PENICILLIN AND CEPHALOSPORIN ANTIBIOTICS

This is a study of the natural production of penicillin and cephalosporin antibiotics by the organism *Streptomyces clavuligerus*. DNA technology is used to increase the production of the *Streptomyces clavuligerus* enzymes which synthesize the antibiotics. If these enzymes can be harnassed as biological catalysts (in cell-free systems) to synthesize many antibiotics, the expensive chemical modifications currently used to enhance antibiotics will be unnecessary. This means more effective and reasonably priced antibiotics.

LEE, Patrick, Ph.D.
Assistant Professor,
Department of Microbiology & Infectious Disease,
Faculty of Medicine, The University of Calgary

Date of Appointment: 81/07/01

THE MECHANISM OF VIRUS ATTACHMENT ONTO HOST CELLS

This is a study of the first step in viral invasion – the way a virus attaches to the host cells. The reovirus (REO, respiratory enteric orphan) found in the human digestive tract is a valuable research model because the virus-cell attachment apparatus (protein σ1) has been identified and the viral gene that codes for this attachment protein is easily isolated.

It is believed that the virus gains entry into the host cell by first anchoring itself via the attachment protein σ1 onto specific "receptors" on the host cell membrane. Using monoclonal antibody production and genetic engineering, Lee is investigating the biochemical nature of the virus attachment apparatus and the cellular receptor. Understanding the process is a step in the future development of antiviral measures designed to block cell-virus interactions at the plasma membrane level.

LEFEBVRE, Yvonne, Ph.D.
Assistant Professor,
Department of Biochemistry,
Faculty of Medicine, The University of Calgary

Date of Appointment: 82/07/01

PASSAGE OF STEROID AND THYROID HORMONES ACROSS THE NUCLEAR ENVELOPE OF MAMMALIAN CELLS

This is a study of why some breast carcinomas are unresponsive to steroid hormone treatment. Currently hormone manipulations cause regression in about 25 percent of breast carcinomas. Because steroid hormones interact with the gene, they must enter the nucleus via a double membrane system, the nuclear envelope which forms a barrier between cytoplasm and nucleus.

Lefebvre hypothesizes passage across this nuclear envelope may be defective in unresponsive tumors. She is investigating the molecular mechanisms by which steroids traverse the nuclear envelope of normal mammalian target and non-target cells, as well as steroid responsive and steroid-unresponsive neoplastic cells.

LEUNG, Wai-Choi, Ph.D.
Associate Research Professor,
Department of Medicine,
Faculty of Medicine, The University of Alberta

Date of Appointment: 82/07/01

MOLECULAR CLONING OF VIRAL NEUTRALIZATION ANTIGEN AND HUMAN TUMOR ANTIGEN

This is a study of ways to use molecular genetic technology to produce effective vaccines for virus-induced diseases. Experimental vaccines recently developed for herpes simplex virus and influenza virus seem effective. However, the minute amounts of neutralization antigen that can be isolated from purified virus prevents large-scale production of the vaccines. Leung is mass producing the virus neutralization antigens in genetically-engineered microorganisms which should reduce production costs and possible hazards.

A second project focuses on the molecular cloning of an antigen associated with human melanoma (pigment-bearing malignant tumors). By identifying the molecular structure of the gene for the antigen (known to be a glycoprotein on the tumor cell surface), the antigen could act as a marker to study tumor development.

MANNONI, Patrice J., M.D.
Associate Professor, Department of Pathology,
Faculty of Medicine, The University of Alberta

Date of Appointment: 82/10/01

ANTIGEN CHARACTERISTICS OF HEMATOPOIETIC STEM CELLS

This is a study of how normal and leukemic blood cells differ in development and structure. Mannoni studies surface membrane markers using monoclonal antibodies produced *in vitro* by mouse cells immunized against leukemia or normal cells and infused with tumor cell lines. Cell culture techniques allow him to study the possible expression of these markers during normal and leukemic cell proliferation. Mannoni is looking for what are called "oncogenes", little understood genes which some scientists believe may undergo change when cancer occurs, or which may be caused by the cancer. The project also includes an investigation of how the membrane markers are modified by external agents such as interferon.

MATHESON, David S., M.D.
Assistant Professor, Department of Pediatrics,
Faculty of Medicine, The University of Calgary

Date of Appointment: 81/07/01

ALTERATIONS IN IMMUNE REGULATION AND CELL-MEDIATED IMMUNITY INDUCED BY VARIOUS FORMS OF INTERFERON

This is a study of how interferon affects natural killer (NK) cells. These white cells have a special ability to kill other cells that have been infected by a virus or become malignant and their activity varies according to naturally occurring factors or drugs. Several patients with cancer have markedly depressed NK activity, but it is not known if this is cause or effect.

Matheson is testing the effects of two types of interferon on NK, as well as other immune functions, and he has found in some patients interferon leads to decrease in NK. He is also investigating how some drugs influence DNA metabolism and how changes in the DNA building blocks affect the level of NK activity.

McFADDEN, Grant, Ph.D.
Assistant Professor, Department of Biochemistry,
Faculty of Medicine, The University of Alberta

Date of Appointment: 81/01/01

MOLECULAR BIOLOGY OF TUMORIGENIC SHAPE FIBROMA POXVIRUSES

This is a study of the molecular interplay between one particular tumor promoting virus, the poxvirus in rabbits, and its target cell. This virus is the only DNA tumor virus which does not exert its effect from a location in the cell nucleus. It can be studied in tissue culture cells grown in the lab.

McFadden is attempting to dissect out the viral genes responsible for the virus's oncogenic potential and to analyze those genes using recombinant DNA cloning and DNA-mediated gene transfer. Since the poxvirus has never been systematically studied at the molecular level before, this research may clarify how a mammalian cell transforms itself into an unregulated and rapidly-dividing tumor cell.

MILLER, Rodman, Ph.D.
Assistant Professor, Department of Anatomy,
Faculty of Medicine, The University of Calgary

Date of Appointment: 81/10/01

FREEZE FRACTURE LOCALIZATION OF ANTIGENS AND OF CHOLESTEROL

This is a study of the development of freeze fracture techniques to identify specific structures in membranes; currently the technique, called freeze fracture electron microscopy, yields a picture of individual proteins as particles imbedded in a (fractured) biological membrane. However, it has not been possible to associate a size or shape of a membrane particle with a particular protein. Miller is developing a technique which uses dyes bound to biologically active materials and an argon laser to selectively heat regions of the membrane. The procedure should allow scientists to specify the molecular identity of objects seen through freeze fracture.

This technique will have many applications in medical research because investigators will be able to locate membrane receptors in a variety of tissues. Miller will apply the method to locate neurotransmitter receptor cells in the retina.

In a second aspect of his research, Miller is using a cholesterol binding drug to locate cholesterol in biological membranes.

MOORE, Graham J., Ph.D.
Assistant Professor,
Faculty of Medicine, The University of Calgary

Date of Appointment: 82/07/01

THE SYNTHESIS AND EVALUATION OF PEPTIDE HORMONES AND ANALOGUES

This is a study of how two peptides, angiotensin and vasopressin, function in normal and abnormal states. Because both these peptides are involved in hypertension and heart failure, Moore is searching for ways to eliminate their undesirable effects in cardiovascular diseases. He is studying the biosynthetic pathways which give rise to the peptides and how they act at their tissue receptors.

This information prepares the way for synthesizing peptides which correct the negative action and could then be incorporated into drugs for the diagnosis and treatment of heart failure.

MOSSMAN, Timothy R., Ph.D.
Assistant Professor, Department of Immunology,
Faculty of Medicine, The University of Alberta

Date of Appointment: 81/01/01
End of Appointment: 82/12/31

RESPONSE OF THE MOUSE TO THE CHICKEN MHC AND STRUCTURAL BASIS FOR IMMUNOLOGICAL RESPONSE OF THE MOUSE TO CHICKEN MHC

This was a molecular study of the immune system by examining how mice respond to chicken Major Histocompatibility Complex (MHC) (histoincompatibility occurs when a graft from a donor is rejected by the host). A second aspect of his research included an investigation of the structural basis for immunological specificity to further understand exactly how an antibody reacts with chemicals called haptens and or carrier proteins to produce an immune response. Mossman also investigated the formation of T cell molecules and protein secretion.

PARSONS, Howard, M.D.
Assistant Professor, Department of Pediatrics,
Faculty of Medicine, The University of Calgary

Date of Appointment: 82/09/01

ABSORPTION AND METABOLISM OF LONG CHAIN FATTY ACIDS

This is a study of how nonessential fatty acids affect the absorption and utilization of linoleic acid. Linoleic acid is the major essential fatty acid which, like other essential fatty acids, cannot be synthesized by humans and must come from food. It is necessary for growth, normal cell function and other body processes.

Linoleic acid is one of three fatty acids in the oral triacyglycerals usually given to people with essential fatty acid deficiency, but scientists don't know how the nonessential fatty acids affect the essential ones.

QUANDT, Fred N., Ph.D.
Assisant Professor,
Department of Medical Physiology,
Faculty of Medicine, The University of Calgary

Date of Appointment: 82/08/12

ELECTRICAL PROPERTIES OF ISOLATED RETINAL NEURONS

This is a study of the processes which generate electrical signals in neurons. Complex electrical activity in neurons is generated by membrane pores which open in response to various stimuli including transmembrane voltage and neurotransmitters. Quandt measures electrical currents caused by ion flow through pores in a small patch of neuronal membrane. He is working towards a theory which will explain the chemical reactions underlying the operation of those pores.

This basic research will help scientists understand diseases of the nervous system such as epilepsy, dementia, congenital disorders, and psychiatric disorders.

RATTNER, Jerome, Ph.D.
Assistant Professor, Department of Anatomy,
Faculty of Medicine, The University of Calgary

Date of Appointment: 81/10/07

HIGH ORDER STRUCTURE OF CHROMOSOMES

This is a structural study of active and inactive chromatic fibre during the development process whereby cells become differentiated. Basic chromatic fibre contains subunits called nucleosomes. These nucleosomes consist of DNA combined with particular proteins called histones and they can be visualized under the electron microscope. Rattner is studying how the basic chromatic fibres folded to form higher order chromatic structures (chromosomes) during the cell cycle. He is also investigating the changes which occur in these levels of organization during transcription and replication.

This research is part of many studies directed toward understanding normal cell function as a step to understanding disease processes.

REHA-KRANTZ, Linda, Ph.D.
Assistant Professor, Department of Genetics,
Faculty of Science, The University of Alberta

Date of Appointment: 81/01/01

THE BIOCHEMICAL BASIS OF MUTATION

This is a study of DNA polymerase, the key enzyme in DNA replication. The bacteria destroying virus called Bacteriophage T4 provides an ideal research model because DNA polymerase mutants can be isolated and the mutant T4 polymerases can be purified. Mutator DNA polymerases no longer replicate DNA accurately and Reha-Krantz is studying them to learn more about the molecular mechanisms controlling accurate and inaccurate DNA replication. Each time a cell reproduces, it is essential that the genetic information (DNA) be copied accurately.

Increased spontaneous mutation rates have been observed in tumor cells. Therefore, though this basic genetic study potentially has wide application, it is particularly relevant to understanding carcinogenesis.

RORSTAD, Otto, M.D., Ph.D.
Assistant Professor, Department of Medicine,
Faculty of Medicine, The University of Calgary

Date of Appointment: 81/07/01

MECHANISM OF ACTION OF BRAIN PEPTIDES

This is a study of brain peptides, substances which scientists believe act as chemical messengers between brain cells and probably cells in other organs. Rorstad is investigating the biochemical mechanisms of peptide function in the pituitary gland and nervous system. He specifically studies somatostatin (SRIF) and vasoactive intestinal polypeptide (VIP) using a number of animal research models including cloned cells from pituitary tumors.

Peptide research is of great interest to all investigators because they suspect peptides may be involved in many disorders of the nervous and endocrine system.

SEVERSON, David L., Ph.D.
Associate Professor,
Department of Pharmacology & Therapeutics
Faculty of Medicine, The University of Calgary

Date of Appointment: 81/09/01

REGULATION OF LIPID METABOLISM

This is a study of lipids, substances in the body which are an important source of oxidative energy in cells and which play a role in diseases like atherosclerosis. Severson is investigating factors which control lipid metabolism. If he can identify metabolic interventions that would decrease lipid activity in heart tissue deprived of oxygen, new therapies could be developed to reduce damage following a heart attack.

He is also studying lipid metabolizing enzymes in arterial tissue to understand the biochemistry of atherosclerosis. Once enzyme regulation is understood, scientists may be able to influence it and retard the build-up of plaque deposits which clog the arteries.

SMITH, Peter, Ph.D.
Assistant Professor, Department of Pharmacology,
Faculty of Medicine, The University of Alberta

Date of Appointment: 81/07/01

ELECTROPHYSIOLOGICAL STUDIES OF THE ELECTROGENIC SODIUM PUMP IN SYMPATHETIC GANGLIA AND SPINAL CORD

This is a study of the enzyme sodium potassium ATPase. All of the electrical activity in the nervous system depends ultimately on this enzyme. Smith uses electrophysiological and biochemical techniques to see if sodium potassium ATPase is altered by neurotransmitters such as noradrenaline and adrenaline, food dyes which may be toxic, the anti-convulsant drug, phenotoin, and various endogenous compounds such as steroids.

Disease states such as epilepsy, alcoholism, manic depression psychosis and infant hyperkinetic syndrome appear to involve this enzyme and the drugs used to treat these problems interact with the enzyme. This work is relevant to our understanding of neurological disorders such as epilepsy as well as certain psychological disorders.

TAYLOR, Diane E., Ph.D.
Associate Professor,
Department of Medical Microbiology,
Faculty of Medicine, The University of Alberta

Date of Appointment: 81/07/01

CHARACTERIZATION OF BACTERIAL PLASMIDS

This is a study of antibiotic resistance in bacteria which cause food poisoning and severe infection in blood and organs of both man and farm animals. In recent years bacteria have become increasingly resistant to antibiotics, probably due to their frequent use in clinical medicine and in livestock rearing. Taylor is investigating how bacterial resistance develops, the mechanisms involved, and how resistance can be eliminated from bacteria. Recombinant DNA and cloning are employed to focus on individual bacterial genes which specify antibiotic resistance.

This study will provide the basis for improved antibiotics and clinical treatment of infectious diseases.

TYLER, Jonathan M., Ph.D.
Assistant Professor, Department of Genetics,
Faculty of Science, The University of Alberta

Date of Appointment: 81/08/01

STRUCTURE AND FUNCTION OF BIOLOGICAL MEMBRANES

This is a study of human red blood cell disorders to understand the molecular basis of specific heritable diseases. Certain diseases of the connective tissue (spherocytosis, stomatocytosis and others) affect red cell shape and function. Tyler is analyzing the network of proteins called the cytoskeleton which controls the shape of the red blood cell. Using the techniques of molecular genetics, he investigates both normal and diseased cells, specifically analyzing the structure of spectrin because a mutation of this protein has been related to abnormal cytoskeletal function.

If Tyler can accurately identify the molecular mechanism of the diseases, the information can be used to develop new clinical treatments.

WAISMAN, David M., Ph.D.
Assistant Professor,
Department of Medical Biochemistry,
Faculty of Medicine, The University of Calgary

Date of Appointment: 82/08/01

STUDIES OF CALCIUM BINDING PROTEINS

This is a study of the calcium proteins fundamental to the second messenger system which activates cell function. Calcium concentration rises in a normal, activated cell, but if there is too much calcium the cell dies and tissue is damaged.

Waisman is examining whether the most well-known calcium binding protein, calmodulin, is the primary intercellular receptor and whether or not there are other binding proteins. He is also investigating the calcium binding activity of heart and brain tissue.

These basic studies have wide application to many disease states which appear to be accompanied by abnormal concentrations of calcium, problems such as muscular dystrophy and some heart disease.

WALSH, Michael P., Ph.D.
Assistant Professor,
Department of Medical Biochemistry,
Faculty of Medicine, The University of Calgary

Date of Appointment: 82/09/01

ENZYME REGULATION BY CALCIUM

This is a molecular study of the biochemical mechanisms which control smooth muscle contractions. Walsh is investigating the second messenger system which activates cell function. He is specifically studying two identified second messengers, calcium which is mediated by the protein calmodulin, and cyclic AMP which is mediated by cAMP dependent kinase. In addition to studying how these processes control smooth muscles, Walsh is searching for new calcium binding proteins.

Smooth muscles in the body include the intestine, vascular muscle, uterus, trachea, esophagus and stomach. If this basic study yields information on how smooth muscles operate, scientists will better understand their malfunctions in conditions such as hypertension, muscular dystrophy, malignant hyperthermia, certain gastrointestinal, respiratory and cardiac disorders.

WENMAN, Wanda M., M.D.
Associate Professor, Department of Pediatrics,
Faculty of Medicine, The University of Alberta

Date of Appointment: 81/07/01

HUMAN INFECTIONS WITH CHLAMYDIA TRACHOMATIS

This is a molecular study of *Chlamydia trachomatis*, a specialized bacteria which causes a variety of human infections such as the eye disease trachoma. *C. trachomatis* is a major agent of venereal disease, more common than gonorrhea, and linked to a still expanding spectrum of disease. Infants born to infected mothers frequently develop pneumonia or eye infections.

Wenman uses recombinant DNA techniques to compare different strains of Chlamydia, investigate potential reagents for rapid diagnosis, and study the feasibility of vaccines.

POOR

QUALITY

ORIGINAL